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PROGNOSIS IN BRONCHIECTASIS

BY

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In 1927, we published in this journal[1] a communication embodying the results of our experience of bronchiectasis in childhood. We then expressed doubt regarding the correctness of the view held by some authors that the condition is curable. Nobecourt[2], for example, in support of Hutinel[3], has stated that recovery not infrequently does take place. This, he thinks, is brought about by the dilatation of the bronchi ceasing to increase, and, as the lung grows, the bronchi ultimately coming to have the normal proportions. Hutinel believed that the younger the age at which the bronchiectasis appeared the more likely was a cure to result. Thursfield and Paterson[4] more recently have re-affirmed this favourable prognostic outlook.

So far as we could see at the time of our first analysis the condition tended to get worse. From a study of the post-mortem material it was difficult, if not impossible, to understand how recovery could take place. Many of the lungs had the naked-eye appearance of a sponge or a hydatidiform mole. Naturally, of course, the post-mortem examples would be the most severe, though it is only fair to state that in several cases death had resulted from operative interference and not in consequence of advancing pulmonary involvement. We also mentioned in support of our scepticism of a possible cure that Sir Andrew Clark[5] and Wilson Fox[6] remarked on the relative infrequency with which the condition was met with during adult life, a fact which these writers took to indicate that in the main life was shortened. They estimated the average duration of life after the inception of bronchiectasis at 11·8 years.

No one to-day will deny that the great difficulty in the past of deciding on the matter of prognosis in bronchiectasis was the uncertainty of diagnosis of the mischief by ordinary physical examination. As Armand Delille[7] has stated, and we have been able to confirm, there are examples with signs but no symptoms, examples with symptoms but no signs, and examples with neither signs nor symptoms. It must be remembered also that amphoric breathing and whispered pectoriloquy, the two classical signs, may be present in the absence of any bronchiectasis. In fact, it is only with the aid of intratracheal injections of lipiodol that a definite diagnosis of bronchiectasis can be made in any individual case. Not only in this way can the presence of bronchiectasis alone be categorically affirmed but also, and this is a matter of prime importance, can the degree of bronchial dilatation be appreciated. It was on these grounds that we expressed the opinion in 1927 that 'the truth regarding the course of this disease is reserved for the future.'

Since 1924, when we first practised intra-tracheal injections of lipiodol as a routine aid to diagnosis in all cases of suspected bronchiectasis, we have kept

in touch with all the examples recognized, and in the present communication we wish to record our findings in the light of this special experience.

In all, we have had under observation 32 definite examples of bronchiectasis. Of these, 12 have died, one of a coincident tuberculous meningitis and four following operation for drainage of the lung cavities or attempted excision of the lung. The average duration of life after the inception of the disease in the remaining seven fatal cases was 2·63 years. Of those still alive, 14 have been under continuous observation for periods varying between three and six years and it is from an analysis of the findings in these cases that we wish to gain information regarding the disappearance or otherwise of a previously existing dilatation of the bronchi. For purposes of better comparison the children have been arranged in groups according to the length of time they have been under observation since the date of the first lipiodol injection.

Group 1.—Children under observation between six and seven years. This group comprises only one child whose history was recorded in our article published in 1927.

Case 1,—A. McM., (3)*, a girl, came under observation on October 2nd 1924, at the age of 7 years on account of a persistent cough and profuse yellow sputum. She had had pneumonia after measles when 21 months old and since then cough and spit had been present, and although varying in severity had on the whole got worse. At times blood was present in the sputum. She had been resident in a sanatorium at the age of 5 years because she was supposed to have pulmonary tuberculosis.

In 1924 she was undersized with a height of 106·5 cm. and a weight of 13·4 kgrm. Her colour was good but the fingers and toes were clubbed. The Pirquet test was negative. The cough was troublesome and came on after the least exertion, and the sputum, which seemed to be brought up in mouthfuls, varied in a day between 2 and 5 oz. The sputum consisted of liquid greenish pus and was devoid of all odour. The left side of the chest was flattened and dull to percussion in the lateral region and over the back below the angle of the scapula. The gastric crescent was on a level with the fifth rib and the heart was drawn over to the left with the apex in the 5th space 4½ in. to the left of the midsternum. The R.M. was tubular at the apex and deficient at the base. After 'posturing' and the evacuation of about ½ oz. of liquid pus the dullness at the left base was less intense, the R.M. became amphoric and pectoriloquy was audible in the region of the angle of the scapula. X-ray examination of the chest showed a distinct honeycomb appearance in the lower half of the left chest, and after lipiodol, an extreme degree of saccular dilatation of the bronchi of the left lower lobe.

She was seen again on Feb. 2nd, 1927. At this time the symptoms were apparently much the same and the cough and spit as bad as ever. The dullness over the left side and the displacement of the heart were unchanged. On inversion, ½ oz. of odourless sputum was evacuated. The X-ray examination after lipiodol was repeated and showed the dilatations to be more marked.

On April 25th, 1930, the mother reported her to be better, but lipiodol demonstrated the bronchiectasis to be still more extensive. The cough, however, was apparently less troublesome and the sputum less in amount, and she had been attending school regularly. The physical signs were practically unchanged, pectoriloquy and amphoric breathing being very marked. She was 133 cm. in height and weighed 24 kgrm. A comparison of Figs. 1, 2 and 3 shows in a striking fashion the gradual extension of the mischief during the period of observation.

Group 2.—Children under observation between five and six years. This group comprises five cases all of whom were reported in the original paper.

Case 2.—A.T., (5), a female, aged 3 years and 10 months came under observation on October 7th, 1925, with the complaint that for 2 years and 9 months she had had a cough which, during the last 9 months, had been accompanied by a yellow spit. She had had measles at 1 year

* Numbers in brackets represent the case numbers in the original communication[1].

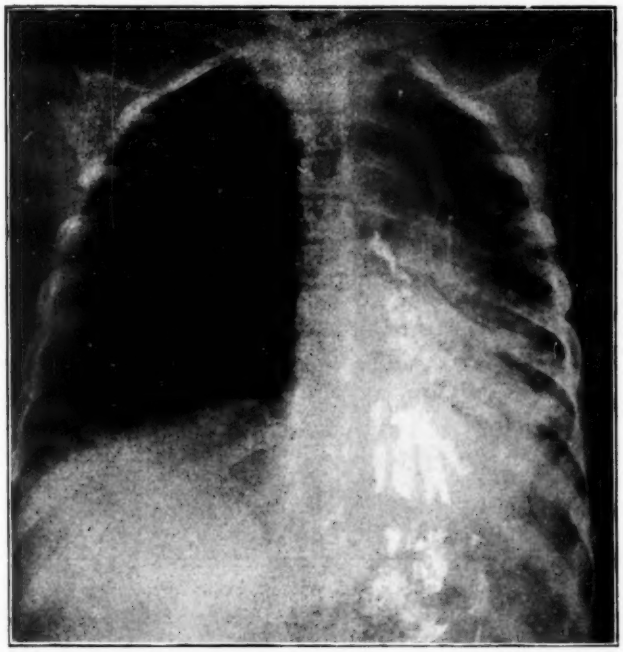

FIG. 1.—Case 1. 6.12.24

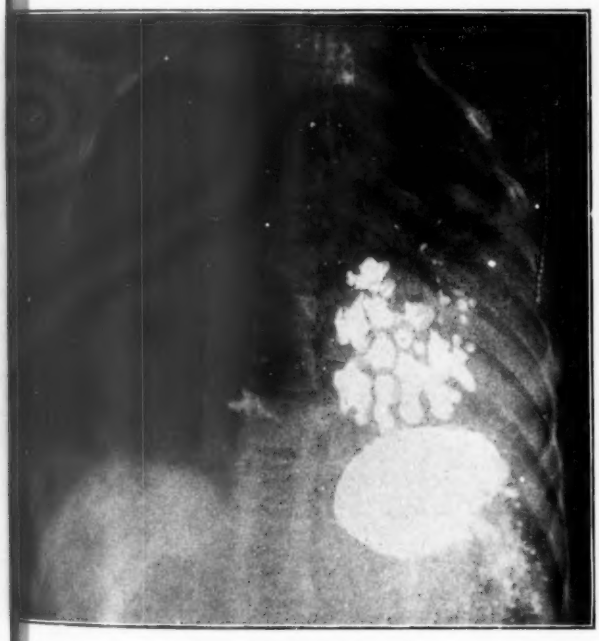

FIG. 2.—Case 1. 10.1.27.

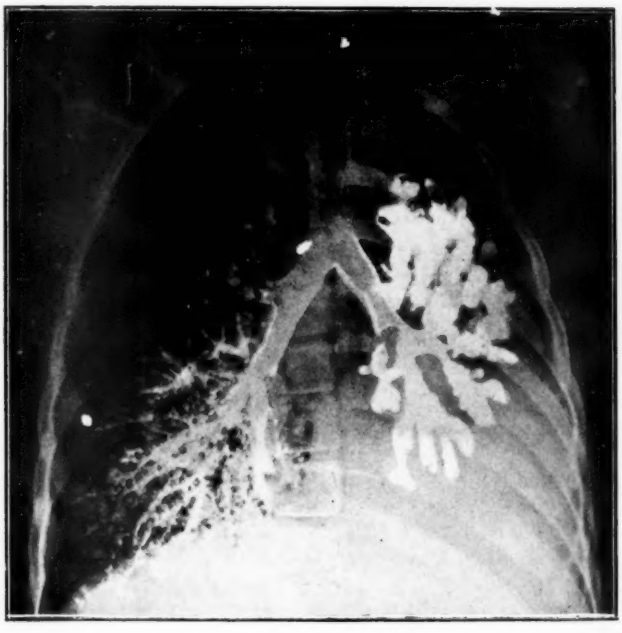

FIG. 3.—Case 1. 26.4.30.

and pneumonia at 2½ years of age. The cough had been present since the attack of measles and the spit since the attack of pneumonia. During the night, but especially on waking in the morning, the child was subject to fits of coughing when she brought up about 1 drm. of pus. Otherwise she appeared perfectly well. She was a healthy looking child of normal height (97 cm.) but slightly under weight (13 kgrm.). The Pirquet reaction was positive. Examination of the chest revealed an impaired note over the right front below the nipple and in the left lateral region. The R.M. was tubular at the angle of the left scapula and was accompanied by much moist râle. After inversion and coughing, ½ drm. of a greenish spit was obtained without

change in physical signs. X-ray examination of the chest revealed a doubtful fibrosis at the left base. Lipiodol demonstrated that the bronchi in both lower lobes, but especially the left, were definitely dilated.

This child was last seen on May 17th, 1930. She had been quite well except for a morning cough during which she brought up about a drachm of pus. Her height was 117·5 cm. and her weight, 19·4 kgrm. The percussion note was impaired at the left base where the R.M. was tubular. After inversion and coughing pectoriloquy became audible. The X-ray examination after lipiodol showed the condition to have become much worse.

Case 3.—P.R., (23), a girl, first came under observation on October 18th, 1922, at the age of 7 years and 10 months with a history of a cough since before she was one year old. At 3 years of age she had had broncho-pneumonia and since then the cough had been worse, coming in bouts and lasting for as long as an hour at a time. No history of sputum was obtained. At the age of 7 years she again had pneumonia and according to the doctor who attended her the left lung did not clear up. On admission to hospital she was an undersized child measuring 102 cm. and weighing 12·1 kgrm. The left chest was found to be smaller than the right, with dullness to percussion at the left apex and over the left lower lobe where the R.M. was defective and tubular. An X-ray examination of the chest revealed a dense shadow all over the left side of the chest with a somewhat honeycomb appearance at the apex. The heart and trachea were displaced to the left.

She was seen again on June 4th, 1925, when aged 11½ years. During the interval the cough had persisted and there was still no history of sputum, but on posturing 2 drm. of a thick muco-purulent odourless expectoration were obtained. She weighed 19·1 kgrm. and measured 111·5 cm. There was still dullness over the left side with an amphoric R.M. in the lateral region. An X-ray examination on this occasion still showed a dense shadow all over the left side with clearer areas at the apex suggesting cavitation. The heart and trachea were displaced to the left. Injection of lipiodol at this time demonstrated definite bronchiectasis in the left lower lobe.

On April 25th, 1930, she was seen again. She was now 16½ years old. On the whole she had been better in her general health but the cough and spit had persisted and she was occasionally dyspnœic. Menstruation had begun at 14 years. The left chest was flat and shrunken with deficient movement. The apex beat was best felt in the 5th space, 5½ in. to the left of mid-sternum. There was dullness over the left back and in the left lateral region with amphoric R.M. and pectoriloquy. The X-ray after lipiodol showed an increase in the cavitation on what had been present in 1925 and a superadded scoliosis.

Case 4.—J.B., (18), a boy aged 4 years when he was first seen on Feb. 25th, 1925, with a history of having had 6 months previously an acute illness characterized by cough, dyspnœa and vomiting. An X-ray one month after this acute illness revealed a shadow throughout the left lung with the heart drawn over to the left. The condition was diagnosed as an unresolved pneumonia. He was slightly undersized, weighing 13·75 kgrm. and measuring 94 cm. He had a troublesome cough but no history of spit. There was dullness to percussion all over the left side of the chest with amphoric R.M. in the axilla and moist râle all over. X-ray examination showed a shadow throughout the left lung with slight tubular clear areas suggestive of bronchi towards the base and a honeycomb appearance at the apex. After the injection of lipiodol, saccular dilatation of the bronchi throughout the left lung was revealed (Fig. 4).

In Feb., 1929, his condition was unchanged. He was still coughing but without spit; his colour was good and there was no clubbing of the fingers. He was 118 cm. tall and weighed 21 kgrm. There was diminished expansion on the left side of the chest with an impaired note in the left lateral region and left front. The R.M. was tubular and pectoriloquy was heard in the axilla. Lipiodol demonstrated the dilatation to be more marked than four years previously (Fig. 5).

In March, 1930, artificial pneumothorax was induced, when it was found that the cavitation could be in great part obliterated (Fig. 6).

Case 5.—J.F., (17), a boy aged 9 years, came under observation on August 15th, 1925. He had had influenza at 3 and measles and whooping-cough at 4 years of age, since when he had been troubled with a cough and subject to febrile attacks. He came under observation during a febrile attack. He was an undersized boy measuring 108 cm. and weighing 17·2 kgrm. His colour was good and there was no clubbing of the fingers. The Pirquet tuberculin reaction was positive. The percussion note was dull at the right base behind below the angle of the

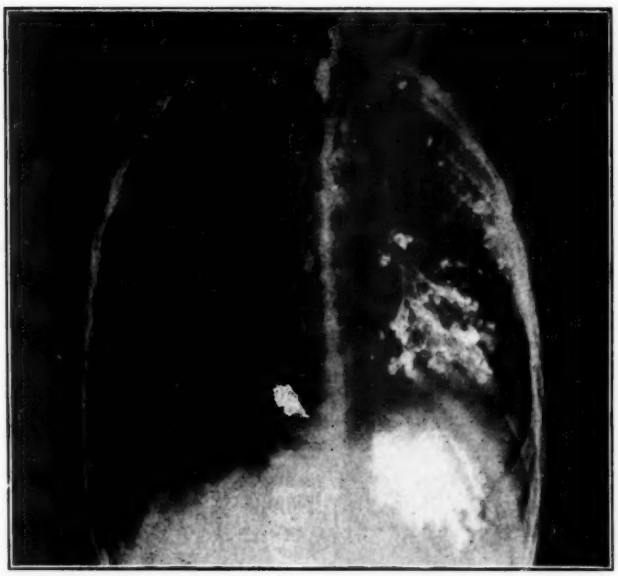

FIG. 4.—Case 4. 21.3.26.

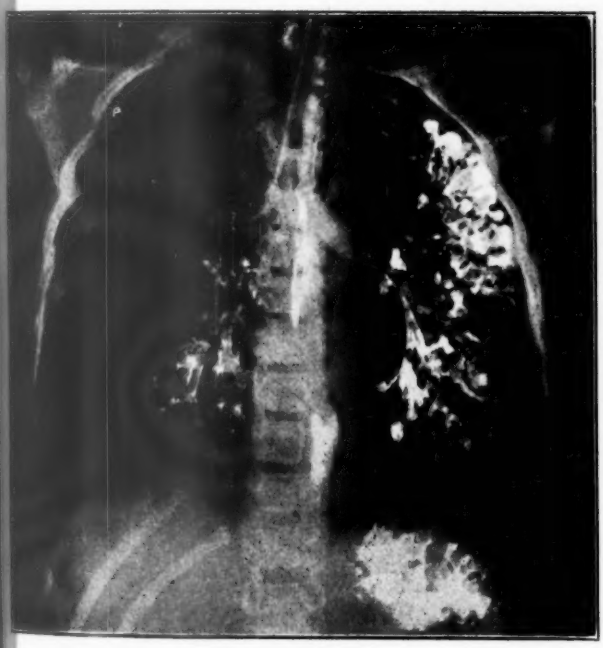

FIG. 5.—Case 4. 2.2.29.

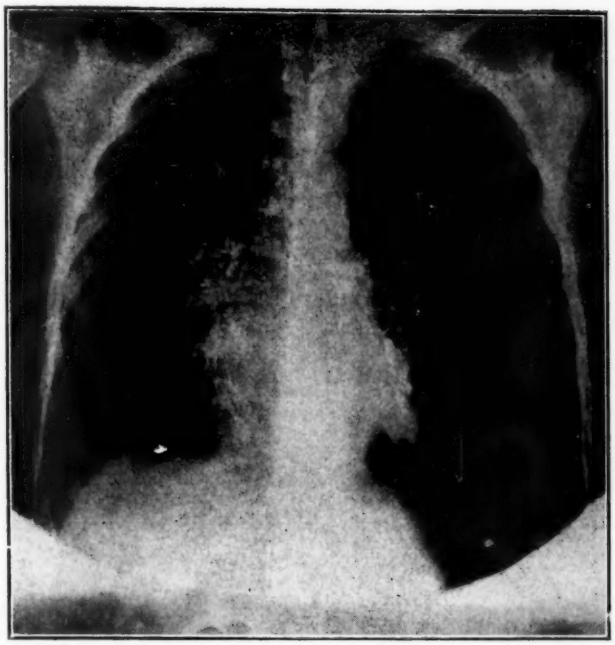

FIG. 6.—Case 4. 6.3.30.

scapula with a very deficient R.M. After posturing 1 drm. of thick purulent sputum devoid of all odour was evacuated, and the dullness at the right base became less intense and the R.M. tubular. X-ray examination revealed widening of the mediastinum and a shadow at the right base; and after lipiodol, a slight but definite degree of dilatation of the bronchi in the right lower lobe.

He was seen again on Jan. 31st, 1929, when he was said to be well, eating and sleeping well, and playing normally. He still had a cough but no spit. The physical signs were negative for disease.

On March 28th, 1930, he still looked well but had a dry unproductive cough. The physical examination was negative, and X-ray examination after lipiodol did not reveal any bronchiectasis.

Case 6.—J.C., (15), a boy first came under observation at the age of 4 years with a history of whooping-cough at one year, and cough and spit ever since. At 3 years he had contracted measles and since then the cough and spit had been worse. The spit latterly had been frequently streaked with blood, and at times there had been definite hæmoptysis. The Pirquet tuberculin reaction was positive. The chest was pigeon-shaped, with dullness at the right base behind and in the right lateral region and abundant moist râles at both bases. X-ray examination revealed shadows at both bases and an appearance suggestive of cavity at the right base.

In August, 1925, at the age of 6 years, he was still troubled with cough and spit, especially at night or after violent exercise. His height was 102 cm. and weight 15·4 kgrm. There was dullness to percussion over the left back and front, and X-ray examination revealed slight honeycomb shadows at both bases with the suggestion of cavity at the right base. Lipiodol revealed moderate tubular dilatation of the bronchi in the left lower lobe. Otherwise the conformation of the bronchi seemed normal.

He was seen again in April, 1930. Cough was still troublesome and there was some spit. The percussion note was impaired at the left apex in front and at the left base behind. The R.M. over the back was definitely tubular where the whispered voice was also well heard. After inversion and coughing no change resulted in the physical signs. Lipiodol on this occasion did not reveal any definite bronchiectasis, though one year previously (April, 1929) the dilatation seemed as marked as it had been in 1925.

Group 3.—Children under observation between three and four years. This group includes three children all of whom were also the subject of discussion in the original paper.

Case 7.—C.C., (9), a boy first seen in November, 1925, at the age of 4 years and 10 months. He had had measles and whooping-cough at one year, and a cough and purulent spit since then. The cough and spit were worse in the evening. There was no fever and the Pirquet reaction was negative. His height was 97 cm. and weight 13·1 kgrm. The fingers were clubbed. Expansion of the left lung was diminished and there was dullness to percussion all over the left side, back and front, and in the lateral region. The R.M. was deficient especially in the axilla where it was tubular. On posturing, 3 drm. of purulent sputum were obtained, following which the R.M. became highly tubular in the axilla and lateral region. X-ray examination of the chest showed a honeycomb shadow all over the left side with the heart drawn to the left. Lipiodol injection revealed bronchiectasis at the left base.

He was seen again on Feb. 21st, 1930. He was able to run about but was dyspnœeic. The cough came and went. There was no sputum. Cyanosis of the lips and clubbing of the fingers were present. The percussion note was impaired at the left base but there was no amphoric breathing nor pectoriloquy but much râle was present. Lipiodol at this time showed a marked increase in the degree of dilatation of the implicated bronchi.

Case 8.—T.M., (12), a boy, came under observation on May 14th, 1925, when 9 years old. He had had whooping-cough at the age of 2½ years and there had been present ever since a cough accompanied by a profuse yellow spit. Five months previously he had developed a right-sided pneumonia followed by empyema which was drained and healed satisfactorily, but as the cough persisted, and in fact was becoming worse, and the purulent expectoration more profuse, he was referred to the medical side for an opinion. At this time he was a healthy looking boy but much undersized, measuring 105 cm. and weighing 24 kgrm. He had a good colour and there was no clubbing of the fingers. The Pirquet test was negative. Examination of the chest revealed an impaired note at the left base with a tubular R.M. at the angle of the scapula. The right chest was clear. After inversion and coughing up ½ oz. of muco-purulent expectoration devoid of all odour, the percussion note at the left base became clearer, the R.M. definitely amphoric in character and pectoriloquy could be appreciated. An X-ray photograph of the chest showed a slight shadow at the left base and after the injection of lipiodol (May 26th) extensive dilatation of the bronchi of the left lower lobe. This boy was in hospital for 8 weeks during which time his condition remained stationary, the daily amount of sputum varying between 1 and 2 oz. The temperature was normal during the whole residence.

In 1929, artificial pneumothorax with subsequent oleothorax was induced. Lipiodol at this time showed the bronchiectasis not only to be more severe in the left lower lobe but to be

commencing in the right. The cough became less frequent and the sputum less purulent but he was dyspnœic. Later the cough and spit returned as bad as ever.

Case 9.—A.S., (19), a girl first came under observation on March 6th, 1926 at the age of 8 years on account of cough and wasting of 8 months' duration. There was a history of broncho-pneumonia at 15 months and again at 27 months of age, whooping-cough at 2½ years with a slow recovery and broncho-pneumonia at 4½ years at which time she was very ill and has never been well since. Eight months previously she commenced to complain of pain in the left side and developed a cough which was most troublesome on waking in the morning, and was accompanied by a yellow spit. She was an undersized child 109 cm. tall and weighing 15·2 kgrm. There was slight cyanosis but no clubbing of the fingers. The Pirquet reaction was negative. The percussion note was impaired all over the left side of the chest but definitely dull over the back with an amphoric R.M. and crackling râles at the base. On posturing and coughing 2 drm. of odourless sputum were evacuated and the R.M. at the base became intensely amphoric.

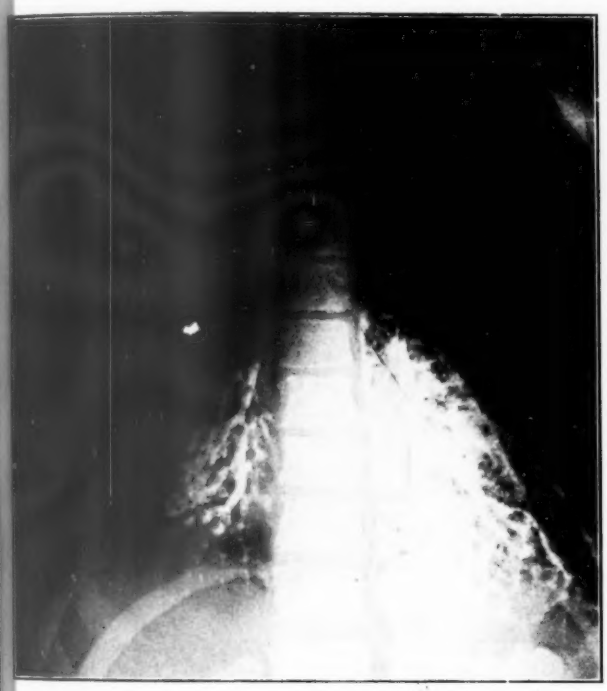

FIG. 7.—Case 10. 13.6.27.

FIG. 8.—Case10. 3.4.30.

The X-ray examination of the chest showed a shadow at the left base with the heart pulled over to the left, and after lipiodol, dilatation of the bronchi of the left lower lobe.

When seen on April 7th, 1930, the cough and spit were unchanged. Otherwise she seemed well. She was a highly coloured girl with cyanosis of the cheeks but no clubbing of the fingers. Her height was 127·5 cm. and her weight 23·4 kgrm. The percussion note was impaired at the left base with defective R.M. and much râle but no pectoriloquy and no amphoric breathing. An X-ray photograph after lipiodol showed the condition to be quite as marked as 4 years previously.

Group 4.—Children under observation between three and four years. The following five cases came under observation during 1927 and are now recorded for the first time.

Case 10.—A.S., a boy, came under observation on June 6th, 1927, when aged 12½ years with a history of cough and spit of 3 months' duration. He had had measles, whooping-cough and pneumonia at the age of 2 years but made a good recovery from these. The cough had gradually got worse and was often severe enough to induce vomiting. He was a big boy, 152 cm. tall and

weighing 29.5 kgrm. The percussion note was impaired at the right base with amphoric breathing close to the mid-line low down, where pectoriloquy was also well heard. 2 c.cm. of sputum were obtained on posturing. The X-ray examination after lipiodol showed a slight but definite degree of bronchiectasis at the right base. This condition had apparently developed spontaneously (Fig. 7).

On April 3rd, 1930, when aged 15½, he was again seen. He was quite well and the cough had disappeared. His height was 167·5 cm. and weight, 48·5 kilos. The percussion note was still slightly impaired at the right base with deficient R.M. but no amphoric breathing or whispered pectoriloquy were heard. Lipiodol injection showed the bronchi to be normal in conformation (Fig. 8).

Case 11.—W.B., a boy, aged 7 years, was first seen on May 5th, 1927 with a history of cough of 6 years' duration. He had had pneumonia at 11 months and again at 18 months, and measles at 21 months. Since the first attack of pneumonia he had had a cough. He was a small boy, 110 cm. in height and weighing 16·8 kgrm. There was an impaired note at both bases

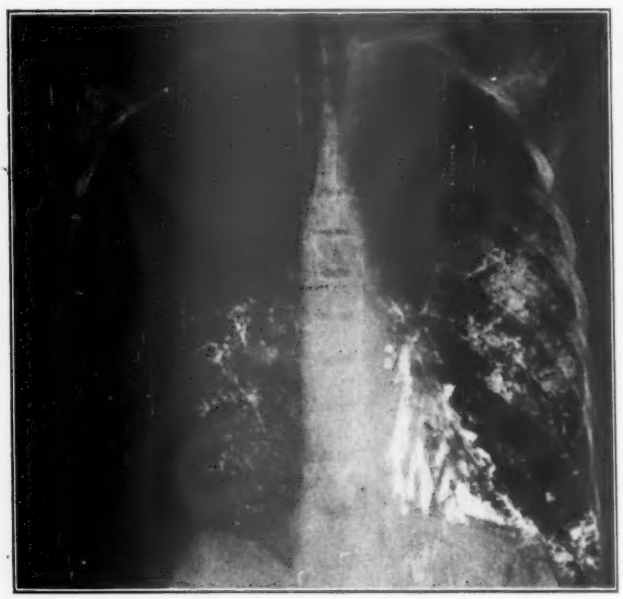

FIG. 9.—Case 13. 28.2.27.

FIG. 10.—Case 13. 1.4.30.

with much moist râle. The whispered voice was well heard at both bases. 2 drm. of fluid greenish pus were obtained on inversion. Lipiodol demonstrated bronchiectasis at both bases.

He was seen again on May 28th, 1930, when it was reported that he was perfectly well except for the cough and spit which had always been present. The physical signs were unchanged. 1 drm. of sputum was obtained on inversion. The X-ray examination after lipiodol showed the condition to be more extensive than in 1927, especially at the right base.

Case 12.—J.McB., a girl, was first seen on May 5th, 1927, at the age of 5 years and 9 months. At 11 months she had had pneumonia and immediately afterwards, measles. She made a good recovery but when 3½ years old began to cough, and this cough had returned each winter since. Just before coming under observation there was a history of hæmoptysis. She was a small child weighing 16·3 kgrm. and measuring 107 cm. in height. On examination of the chest, no dullness could be detected and there was no change in the R.M., but much moist râle at both bases. On inversion, 1 drm. of sputum was obtained. X-ray examination after lipiodol showed a tubular dilatation of the bronchi at the left base.

When seen again on April 29th, 1930, aged 9 years, she was 124 cm. in height and weighed 21·3 kgrm. She still had a cough but only 2 c.cm. of sputum were obtained on posturing. She

looked well and her colour was good. There was slight impairment of the percussion note at the left base where the R.M. was faintly tubular. The lipiodol injection was repeated and revealed the bronchiectatic condition to be practically the same as noted three years previously.

Case 13.—W.McC., a boy aged 7½ years when first seen on Feb. 25th, 1927. He had had broncho-pneumonia when 2½ years old and a cough and spit had been present ever since. At the age of 6, the tonsils and adenoids were removed, and 2 months later he had a second attack of pneumonia followed by measles. The sputum was said to be abundant. He was a small boy weighing 18·6 kgrm. and measuring 113 cm. There was slight clubbing of the fingers. He was highly coloured but not cyanotic. The percussion note was impaired at the right apex in front and at the left base behind. At the left base the R.M. was diminished but no pectoriloquy was audible. The amount of sputum varied from 20 to 50 c.cm. daily. X-ray examination showed slight mottling over the heart area and after lipiodol a slight degree of dilatation of the bronchi at the left base (Fig. 9).

He was seen again on March 31st, 1930. At this time he was up to height for his age (135 cm.) but 1·5 kgrm. under weight. He still had a cough but the spit had disappeared. No clubbing of the fingers could be appreciated although early clubbing was noted 3 years previously. The percussion note was impaired at the left base with a diminished R.M. No spit was obtained on inversion. Lipiodol injection at this time failed to reveal any bronchiectasis (Fig. 10).

Case 14.—A.D., a boy, was first seen on Feb. 12th, 1927, at the age of 9 years because of hoarseness and occasional pain in the chest. He had had measles and whooping-cough but had made a good recovery from these. Two years previously he had had pneumonia but did not fully recover. One year later he again had pneumonia and since then cough has been present. He was a small boy with a height of 122·5 cm. and weighing 22·3 kgrm. His colour was good and there was no clubbing of the fingers. Physical examination revealed impairment of the percussion note at the left base with a tubular R.M. and fine moist râles at both bases. No sputum was obtained on coughing even while in the inverted position. Injection of lipiodol showed extensive saccular bronchiectasis at the left base.

This boy was seen again on July 15th, 1929. His height was then 135 cm., and his weight 27·28 kgrm. The percussion note was still much impaired at the left base but the R.M. was not tubular though there was much fine râle at the left base no sputum could be obtained. X-ray examination after lipiodol showed the bronchiectatic condition to be unchanged.

Discussion.

From a review of the above recorded fourteen cases, all of which have been observed over a longer period than three years, it is seen that a pre-existing bronchiectatic condition can disappear but, be it noted, that in each of the cases (No. 5, 10 and 13) in which this was observed the degree of dilatation was slight.

Our experience does not support Hutinel's contention that the earlier the age at which the lesion appears the more likely is it to recover, since of the three cases which healed the average age at the apparent onset was 6·1 years, in comparison with 3·1 years which was the corresponding age for the whole series. In fact, Case 10, which of the whole series was the child in whom the condition developed latest, namely at 12 years, was one of the children who recovered.

In three cases the condition remained unaltered and in these the average age at which the condition probably appeared was 2·1 years. In the majority of the cases, however, to be exact in 8, the condition steadily got worse. In these cases the average age at which the disease appeared was 2·3 years. When we further recollect that of the total 32 cases of definite bronchiectasis which we have observed 12 have died the prognosis would undoubtedly appear to be on the whole grave.

It might be suggested, and we admit with apparent justification, that it would be the cases of shortest duration which would be most likely to recover.

but so far as the small series which we have been able to collect is concerned little support is lent to such a hypothesis. The average duration of the condition when first observed was in those who recovered 3·4 years ; whereas in those who steadily got worse it was 4·2 years, and one of these had the shortest history in the whole series, namely, 3 months. This apparent though slight supporting evidence was, however, counterbalanced by the fact that one of the cases which steadily got worse had only been ill for 6 months, and many of them had not been of such long duration as two of those who recovered. It would seem rather that it was a matter of the particular cause of the inflammation than the individual age of the pulmonary fibrosis which determined its liability to disappear or progress.

In the following table we have summarized the details regarding the age of onset, duration and termination of the individual cases.

TABLE I.

SUMMARY OF 14 CASES OF BRONCHIECTASIS IN CHILDHOOD.

No. of case	Duration before observation	Age of onset	Result
1	5·0 yr.	1·75 yr.	worse
2	2·75 ,,	1·0 ,,	,,
3	7·0 ,,	1·0 ,,	,,
4	0·5 ,,	3·5 ,,	,,
5	5·0 ,,	4·0 ,,	well
6	3·0 ,,	1·0 ,,	stationary
7	4·0 ,,	1·0 ,,	worse
8	6·5 ,,	2·5 ,,	,,
9	3·5 ,,	4·5 ,,	stationary
10	0·25 ,,	12·0 ,,	well
11	6·0 ,,	1·0 ,,	worse
12	2·5 ,,	1·0 ,,	stationary
13	5·0 ,,	2·5 ,,	well
14	2·0 ,,	7·0 ,,	worse

Conclusions.

1. The prognosis in bronchiectasis in childhood is grave as the condition usually steadily gets worse and leads to a fatal termination.

2. Undoubted bronchiectasis following a chronic pneumonia may disappear but only when the degree of dilatation is slight.

3. The age of onset of the bronchiectasis would seem to influence the course of events : recovery is more probable in the examples which develop during later childhood.

4. During childhood the duration of the illness is of no prognostic help.

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SPINAL TUMOURS IN CHILDHOOD

BY

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Spinal tumours are rare in childhood. Stursberg[1], in a collected series of 116 operated cases, found one in a child under ten, and six between ten and fifteen years of age. Schultze[2] in his series reported one case in a child, while none were noted in the series of Antoni[3], of Flatau[4] and of Nonne[5]. Elsberg[6] had one patient under ten years in his own 100 cases. Byron Stookey[7] found eight cases in children under twelve years out of 165 verified tumours of the spinal cord for which operation was performed at the Neurological Institute, New York, between 1910 and 1926 inclusive. Tuberculomata are probably not so common as was once supposed[7, 11].

The older statistics are from post-mortem records, and show a higher incidence in children. Thus, Horsley and Gowers[8] in their compilation of 58 cases found 10 per cent. in children, and Lloyd and Mills[9] found 12 per cent. Schlesinger[10] in 251 collected cases found 13 per cent. occurring up to the age of nine years, and 11 per cent. between the ages of ten and fifteen.

The discrepancy between the post-mortem and operative groups of statistics suggested, naturally, that spinal tumours have not been recognized readily in children during life.

Case records.

In this paper we report two cases of spinal tumour, the first a cholesteatoma in a boy of eight years, and the second a tuberculoma in a girl of eight years. Both patients were operated upon successfully.

Case 1.—F.W., male, aged 8 years, was sent to the hospital (September 6th, 1930) as a probable case of Pott's disease of the spine. He was the youngest of a family of seven children. The parents were healthy, and there was nothing of note in the boy's past history.

For three years previous to admission he had complained of pain in his back. It was always worse on bending forwards and was first felt when he bent to put on his stockings or tie his bootlaces. It was not constant, but came and went. During the last few months the pain had been worse and more constant, and was often accompanied by a tired feeling in the legs, and a feeling of general weariness. For the last year of the illness, there had been nocturnal incontinence of urine, sometimes once, sometimes twice a week. For about three weeks before admission there had been incontinence almost every night.

He was a well-nourished boy weighing 51 pounds. There was lumbar lordosis, and bending the backforwards caused pain. Pain in the region of the lumbar spine was also caused by flexing

the head on the chest. There was tenderness on heavy percussion over the twelfth dorsal vertebra. Over the fourth lumbar vertebra there was a small dimple in the skin, which was surrounded by a port-wine stain about one inch in diameter. This in turn was surrounded by a brownish area of skin pigmentation. Heart and lungs were normal. There was some weakness of extension at the knee on both sides, and slight weakness of dorsi-flexion of the right foot. The gait was normal, except that the back was held rather stiffly. Apart from hyperæsthesia in both groins, there were no sensory disturbances as regards touch, heat and cold, and pain. No saddle anæsthesia was found. The senses of vibration and passive movement were not impaired. The plantar reflexes were flexor. The abdominal reflexes were elicited easily and the responses were equal on the two sides. The cremasteric reflexes were elicited. The knee jerks were not elicited. The ankle jerks were elicited, and equal on the two sides. There was no ankle clonus. There were no wasting of muscles, and no trophic changes in the skin. Nothing abnormal was noted in the cranial nerves. The fundi of the eyes were normal.

X-ray examination of the spine was negative, except that the shadow of the spine of the third lumbar vertebra in the antero-posterior picture was not so well marked as the spines of the other lumbar vertebræ. A lateral picture, however, showed the lumbar spines to be all about the same size. There was no spina bifida.

Fig. 1. Case 1. Spinal cholesteatoma.

Lumbar puncture gave a cerebro-spinal fluid which was clear and quite colourless, and contained three cells per cubic millimetre. Its globulin was greatly increased. The Wassermann reaction in the fluid, as in the blood, was negative. Quenckenstedt's test was positive.

Operations.—On October 3rd, 1930, under intra-tracheal gas and oxygen and local novocaine anæsthesia, the spinal canal was opened by the removal of the laminæ of the eleventh and twelfth dorsal vertebræ, and of the first to the fourth lumbar vertebræ. The removal of the third and fourth lumbar vertebræ was previously decided upon in case the spinal tumour had a relationship to the dimple in the skin over the fourth lumbar vertebra. The dura mater was joined to the laminæ of the fourth lumbar vertebra by a fibrous band. There was no pulsation of the dura below the level of the eleventh dorsal vertebra. Otherwise the appearances were normal. The wound was closed up.

Five days later the second operation was carried out. The dura mater was incised, and at once a pearly white tumour was seen, which lay in its upper half on the cord, and in its lower half on the cauda equina. As the incision in the dura was extended, the tumour practically delivered itself from the canal, and was readily shelled out from above downwards. It was adherent to the pia-arachnoid by a pedicle at its lower pole. The pedicle was cut, and the tumour removed. The dura was stitched up, and the wound closed in layers.

Report on tumour.—The tumour was a typical cholesteatoma (see Fig. 1). It was spindle shaped, and was 3·6 cm. in length. The pedicle measured 0·7 cm. The maximum breadth was 1·6 cm. It was soft and crumbled readily on handling. It was white, and in places had a

pearly sheen. It gave the impression of a cocoon tending to unroll into thin sheets. Each tip was helical (see Fig. 2), and slightly yellow in colour. A transverse section showed the same structureless pearly white appearance, with occasional yellow patches. The greater part of the tumour dissolved away completely in the preparation of sections for microscopic observation, and the residual substance showed parallel but sometimes interlacing fibres of structureless basophilic material, showing no nuclei at all. The tumour contained 10 per cent. cholesterol.

PROGRESS.—Apart from a pyrexia lasting three days after each of the operations, the recovery was uneventful. The incontinence of urine ceased after the first operation, and did not return. Examination on November 5th, 1930, showed that the power in the legs was good, apart from very slight weakness of extension at the left knee. The knee jerks were still absent. The hyperæsthesia of the groins had disappeared, and the back and head could be bent forwards without pain.

Case 2.—C.S., female, aged eight years and nine months, was admitted to hospital on November 5th, 1929. She was the elder of two children; the other, a boy of 5½ years, was healthy. There was nothing of note in the past history, except an attack of uncomplicated diphtheria at the age of 3½ years. There was no history of trauma.

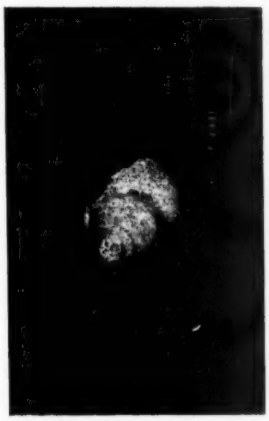

FIG. 2. Case 1. Spinal cholesteatoma.

Eighteen months before admission she began to have attacks of abdominal pain. The pains, probably root pains, usually commenced in the back, and radiated down both sides of the abdomen just below the ribs, and settled usually about the umbilicus. The attacks lasted from a few minutes up to half an hour, and occurred at intervals over a period of six months. The pains then ceased, but the parents noted that the child walked with the right shoulder raised a little, and with the back held stiffly. The spine was X-rayed at this time at another institution, with a view to excluding Pott's disease. Six months before admission she began to complain of pins and needles in the feet, and about this time began to drag both feet a little when she walked. There was no incontinence or retention of urine, and no bowel disturbance. The power of walking steadily decreased, and for a month before admission she was confined to bed.

She was a fair, fine-skinned child, weighing 50 pounds. There was lumbar lordosis, and pain was felt in the back when she bent forwards. Pain in the lumbar region was complained of when the head was flexed on the chest. There was tenderness on heavy percussion over the three lowest dorsal vertebræ. She dragged both legs on walking, and there was a slight toe-drop. There was no wasting of any muscles. Flexion at the hips and at the knees and plantiflexion were good, but there was some weakness of extension at the knees and of dorsiflexion of the feet. The weakness was about equal on the two sides. The muscles of the abdomen, trunk and arms acted well. There was a band one inch wide of hyperæsthesia at the level of the umbilicus, and below this level there was some deficiency of sensation, as tested by cotton wool and the dragged pin. The child objected less to pin-prick over the same area. The temperature sense was

difficult to test, but the answers were certainly less accurate below the level of the umbilicus. The sense of vibration was absent below the twelfth dorsal vertebra. The sense of passive movement was defective in the right leg and foot, and the answers given on testing the passive movement of the left foot were not altogether satisfactory. The plantar reflexes were flexor. The lower abdominal reflexes were not elicited, but the upper abdominal ones were brisk. There was no disturbance of the sphincters of the bowel or bladder. The knee jerks were not elicited. The ankle jerks were elicited on the two sides and equal. The arm reflexes were equal on the two sides. There were no trophic changes of the skin or muscles. The cranial nerves were normal. The fundi of the eyes were normal. Examination of the heart, lungs and abdomen showed nothing abnormal. In particular, there were no evidences of tuberculosis. The cutaneous tuberculin test of von Pirquet was negative.

Lumbar puncture gave a xanthochromic clear fluid which did not clot on standing. It contained four cells per cubic millimetre, and the globulin was much increased. The Wassermann reaction of the fluid, as of the blood, was negative. Quenckenstedt's test was positive. X-ray

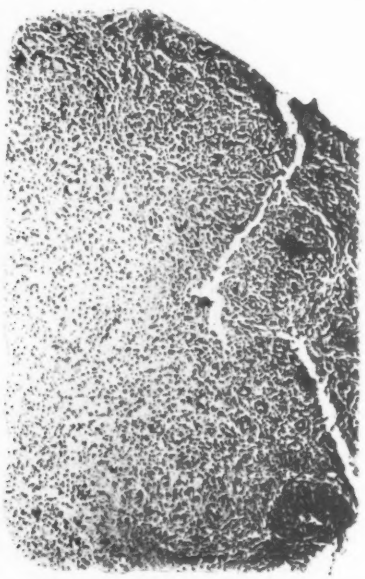

FIG. 3. Case 2. Spinal tuberculoma, microscopic section (×48).

examination of the dorsal and lumbar regions of the spine was negative. The electrical reactions of the leg muscles were normal.

A diagnosis was made of spinal tumour extending from the tenth thoracic to the fourth lumbar segments of the cord.

OPERATIONS.—On November 15th, 1929, under intra-tracheal gas and oxygen, and local novocaine anæsthesia, the spinal canal was opened by the removal of the laminæ of the seventh to the twelfth dorsal vertebræ, and of the first lumbar vertebra. At the level of the seventh vertebra there was definite pulsation of the dura mater noted, but below that level there was no pulsation and the dura was bulging and of a bluish red colour. The wound was then closed up.

Four days later a second operation was done. The wound was opened up, and the dura again exposed. The dura was incised along the whole length of the part exposed, and then it appeared that the cord itself was thickened, red in colour, and obviously very vascular. There was no appearance of a localized tumour. It was not considered that anything further could be done in the way of tumour removal. A small piece of the vascular tissue was removed for examination, the dura was stitched up, and the wound closed in layers.

REPORT ON TUMOUR TISSUE.—Tuberculous granulation tissue, composed mostly of endothelial cells and small round cells. Scanty giant cells also evident (see Fig. 3 and 4).

PROGRESS.—Apart from a pyrexia lasting two days after each operation recovery was good Seven days after the second operation it was found that the knee jerks could be elicited on the two sides, but that the condition was otherwise as on admission. The sense of passive movement slowly returned, the weakness of the legs and feet slowly disappeared, and sensation below the umbilicus improved. When she was discharged on January 29th, 1930 she walked properly without support, and without dragging of the legs. In fact, the only abnormal sign was a slight deficiency of sensation up to the umbilicus. X-ray therapy was considered advisable, and four exposures at monthly intervals were given. On re-examination on November 3rd, 1930, the girl was found to be walking perfectly, and to be running with no apparent effort. The movements of the spine were normal. The area from which the laminæ were removed felt quite firm. A skiagram taken on that date shows signs that are suggestive of the formation of new bone in the places where the laminæ were removed. The general condition of the child is improved. She is attending school as a normal child.

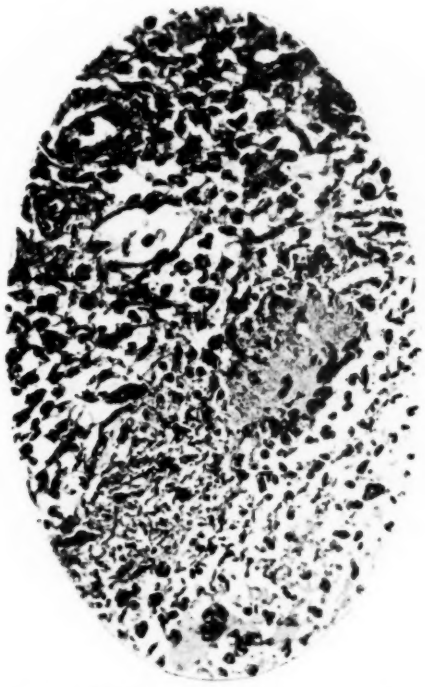

FIG. 4. Case 2. Spinal tuberculoma, microscopic section (×180).

Note on operations.—A laminectomy followed by incision of the dura and handling of the cord is a proceeding that will tax the resistance of a young child to the fullest extent. We believe that a two-stage operation is the method of choice in such cases, and that the best anæsthetic is intra-tracheal gas and oxygen with as little ether as possible, and that infiltration of the operation area with a local anæsthetic combined with adrenalin should be practised.

Both the cases of spinal tumour showed signs of shock after the first operation, and both disturbances of temperature after each operation. It would appear that the removal of the laminæ does not cause any apparent disability of the spine when the bodies of the vertebræ are healthy. In young patients one would expect a certain amount of bone regeneration from osteogenetic cells adherent to the under layer of the periosteum which is pushed off the laminæ but remains adherent to the overlying muscles.

Summary.

1. A case of a spinal cholesteatoma in a boy of eight years is reported. Removal of the tumour was followed by recovery.

2. A case of a spinal tuberculoma in a girl of eight years is reported. Spinal decompression led to recovery.

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A CLINICAL STUDY OF NUTRITIONAL XEROPHTHALMIA AND NIGHT-BLINDNESS

BY

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Amongst the urban population in the industrial districts of northern England there are to be seen occasional cases of night-blindness or xerophthalmia due to diet deficiency. The patients usually come to hospital with the symptom of night-blindness to seek advice from the ophthalmologists, who readily recognize the nature of the disease and give the appropriate treatment without referring them to the physicians. This may in some measure account for the absence of any recent reference to it in this country, for I can find no published records of recent cases apart from those reported from China during the past few years. I do not suggest that China and northern England are unique in this manner, for I believe that the disease is more wide-spread than is commonly believed, and that an appreciation of its early symptoms will lead to its readier recognition by general physicians.

During the past year my colleague, Dr. J. S. Arkle, has given me the opportunity of studying all these cases which have come to his ophthalmological department, where out of a total of 4,100 out-patients there were 17 cases of nutritional night-blindness or xerophthalmia. Getting the clinical material in this way I have had the advantage of having first an expert ophthalmological opinion and report on the cases, and so of avoiding the possible mistake of including in my series patients suffering from night-blindness or corneal ulceration due to causes other than diet deficiency. That the disease was due to a fault in diet was in each case further confirmed by the results of treatment. Careful selection of the clinical material in some such manner is of importance, for after reading some of the accounts of cases which have been published, especially of those in marasmic infants, it is not clear that the diagnosis was fully established, and the condition of corneal ulceration may have been due to causes other than true nutritional xerophthalmia.

The association of night-blindness and diet deficiency was a fact known to the ancients. They even recognized that some cases could be cured by eating liver, and this knowledge is to be found handed down as tribal lore amongst the Esquimaux and other primitive races. But it is only during the past seventy years that this disease has been the subject of careful clinical and experimental studies; full reference to which is to be found in the papers of Mori[1], Ross[2], Bloch[3], and Blegvad[4]. The chief milestones in the advance of our knowledge were the early clinical descriptions in 1866 of von Græfe and

Bitot; the extensive clinical investigations of Mori, who saw 1,511 cases of xerophthalmia and 116 cases of keratomalacia in Japan from 1899 to 1902, and cured them by giving the oil of fishes' liver; and the more recent experimental and clinical studies of Bloch, McCollum and others. As a result of these it is now generally accepted that the disease is due to a specific diet deficiency, which is probably a lack of sufficient vitamin A.

The symptoms vary according to the gravity of the disease and the age of the patients, but in the order of their appearance and severity they usually are: (1) night-blindness, (2) xerosis conjunctivæ with the characteristic Bitot's spots, and (3) keratomalacia. In young infants the disease appears to advance rapidly to the stage of keratomalacia, in older patients there may be night-blindness without xerophthalmia, but, as Pillat[5] has shown, all stages may be present in adults, and from my experience even young children may have night-blindness only. It is also generally accepted that the anti-xerophthalmic factor is also the growth factor, and in addition has a specific effect of increasing resistance to certain infections. This view is based on experimental work in rats and other animals, but it is not fully confirmed by clinical observation or experiment, and it is not supported by the results of my own studies.

In most records of this disease attention has been drawn to the singular manner in which it has affected patients of a particular age or at a particular season of the year. Nearly all of Mori's cases were children between the ages of 1 and 5 years, and the Danish cases were nearly all under the age of 12 months. In the 17 cases which I have seen there was no definite age incidence. The youngest patient was 2 years and 1 month, the oldest 54, but it was chiefly older children and young adolescents who were affected. The actual ages were: 2, 2, 4, 5, 8, 9, 11, 12, 12, 14, 14, 16, 17, 21, 23, 24 and 54 years. The social conditions were evidently of the poorest. The oldest patient lived alone in a lodging room. The others all came from large families with the parents unemployed, and the average income available for buying food, after deductions for rent heating and insurance had been made, was from 2 to 3 shillings per week per person.

In all the patients above the age of 2 years night-blindness was the first and chief complaint. In 3 cases night-blindness was the only symptom and they had no visible lesions in the conjunctivæ. In the remaining 14 cases there were to be seen the characteristic signs of xerophthalmia in various stages of development. Amongst the boys the matter of most immediate concern was that, as dusk approached, they could not see to compete successfully in play with their companions in the street. In the two youngest patients, both aged 2 years, there was no complaint of night-blindness, and they were brought to the hospital because the parents had noticed the whitish deposit on the scleral conjunctiva. On further examination of these two children in the dusk it was shown that they had some night-blindness, although it had not been noticed by the parents. This suggests that the reason why the disease does not assume such a severe form in adults as in young children is that the adults seek advice earlier for the symptom of night-blindness, and receive curative treatment before further damage is done.

It is the opaque whitish deposits on the scleral conjunctiva which is the most characteristic sign of the disease. Bitot first described them and they are now known as Bitot's spots (Fig. 1). The conjunctiva itself may be dry and lustreless, and on this the spots have the appearance of foam or of frost on window panes. In size they vary from tiny specks to particles big enough to cover the whole scleral quadrant beyond the cornea. They are firmly attached and wrinkle peculiarly as the eye-ball is moved. In the later stages

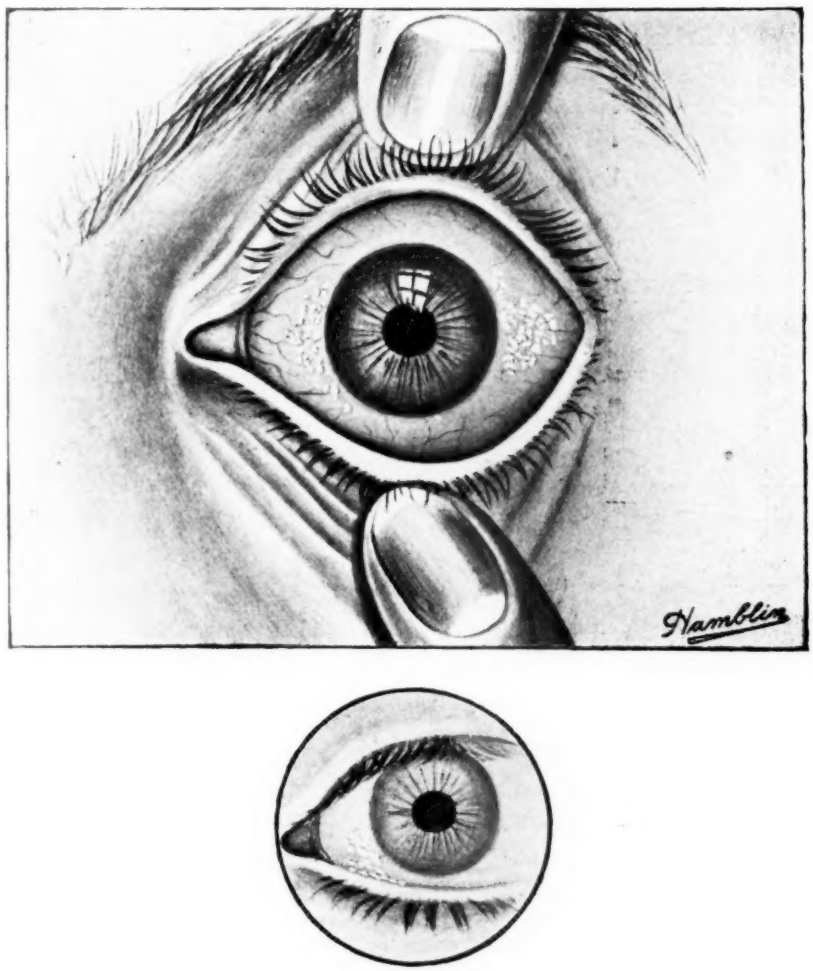

FIG. 1. Appearance of eye in xerophthalmia of moderately severe degree. Bitot's patches on scleral conjunctivæ. (Drawing supplied by Messrs. Theodore Hamblin Ltd.)

there may be some super-added infection, but in most cases this is absent and the patient feels no discomfort in the eye. In four cases there was early keratomalacia, but in each of these there was also well marked xerosis conjunctivæ with Bitot's spots. I saw no case with corneal damage which did not have these well marked signs in the scleral conjunctivæ, and I should hesitate to diagnose nutritional xerophthalmia where the sole evidence is corneal ulceration without Bitot's spots.

There was a history of an evidently deficient diet in all cases, with little or no animal fat or meat protein. A close scientific analysis of a diet which has already been eaten is not possible, but enquiry showed that in almost every case it had consisted mainly of wheat flour bread, margarine, jam, vegetables and tea, but of these they had eaten sufficient quantity to satisfy their needs. The deficiency was therefore qualitative, not quantitative. Indeed the amount of bread eaten by some of the boys had been enormous. In no case had milk been drunk apart from the small amount put into tea. A few ounces of meat had been eaten once a week by the majority. Two cases had eaten an egg every day for at least 4 weeks without preventing the onset of the eye symptoms and signs of xerophthalmia. It appears that these eggs at least had no anti-xerophthalmic effect.

There was no definite seasonal incidence in the onset of the disease. Night-blindness was more apparent or became more accentuated in the spring or summer months, but it could not be shown that there was an excess of bright sunshine at those times, and in six cases the symptoms started in the months of December to March. It has been suggested by some observers that the seasonal incidence of night-blindness is partially to be explained by the extra strain of bright sunshine in the summer months amongst people who are already living on a border-line deficient diet, but the circumstances of two cases proved that this was more probably due to the physical exertion of extra work at that time. These were boys of 16 and 17 years. They complained of night-blindness and xerophthalmia with Bitot's spots. The first symptoms had appeared in the months of July and August, but in each case they had started heavy physical work in a coal mine a few weeks before the first symptoms appeared, and being underground most of the day had had little opportunity of being exposed to bright sunshine. Their diet was typical of that likely to produce xerophthalmia, and had been so for many months before they started working in the pits. Thus it appeared that in these cases the precipitating factor was extra physical exertion and not sunshine.

TABLE I.

WEIGHTS, HEIGHTS AND HAEMOGLOBIN VALUES: NORMAL FIGURES IN BRACKETS.

Case No.	Age (years)	Weight (pounds)		Height (inches)		Hb. % (Sahli)
1	2	19½	(27)	31	(34)	45
2	2½	26	(29)	33½	(35½)	72
3	4	37¼	(35)	31	(40)	—
4	5	44	(42)	42	(42)	80
5	8	54½	(55)	48	(48½)	85
6	9	50¾	(57)	46½	(49)	65
7	11	51	(69)	50	(53)	—
8	12	84	(80)	55	(56)	92
9	12	72	(80)	56	(56)	74
10	14	87	(100)	59	(61)	60

On measurement most of the patients were only slightly below the ideal standards in height and weight, and the general condition and appearance was that of fairly robust health (Fig. 2). The youngest child, aged 2, alone looked at all ill. He weighed 19 lb. 8 oz., had a hæmoglobin of 45 per cent., could not walk, and resembled the type described by Bloch as 'carbohydrate dystrophy.' All others had the appearance of well nourished active looking people. In Table I are given the actual weights, heights and hæmoglobin

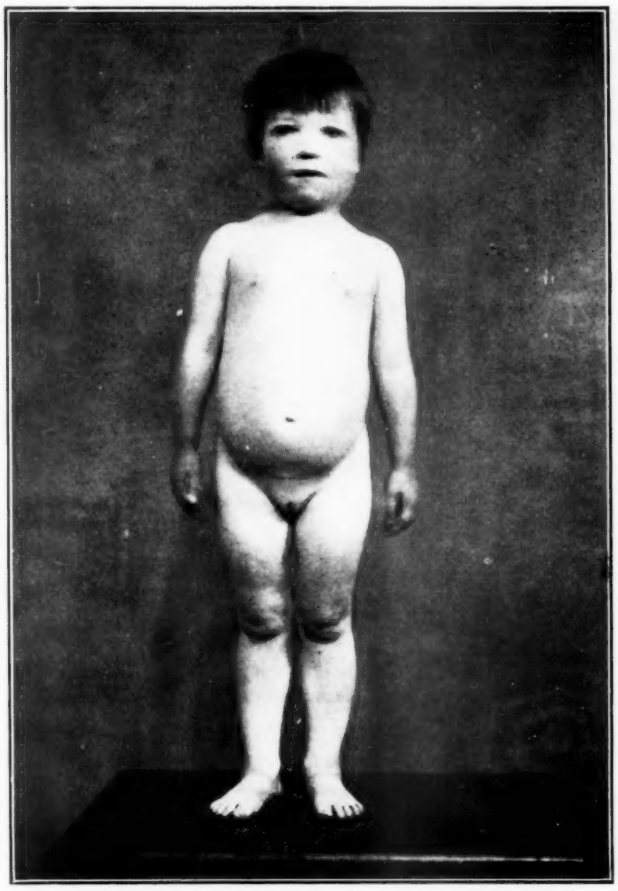

FIG. 2. Child of 2 years and 11 months—with recurrent xerophthalmia for more than 6 months. Bitot's spots in all four quadrants of scleral conjunctivæ. Showing good general condition. Weight 30 lb. (normal 32 lb.). Height 35½ inches (normal 36½ inches).

values of the ten youngest patients, and it will be seen that there is no great divergence from the usual type of hospital patient. There was one prominent symptom, however, of which all the older patients complained, and that was lassitude. It appeared to be a common accompaniment of the disease, and disappeared quickly under treatment. Apart from this and the eye signs there were no other special symptoms.

At this point I may mention the result of treatment in so far as it affected the rate of growth of the patients. There was no striking rise of height curves coincident with the cure of the xerophthalmia such as occurs in experimental animals on a diet deficient in vitamin-A when given curative diet.

Fig. 3 refers to a case of a boy who had had symptoms of xerophthalmia for 6 months and had been on a poor diet for some time before that. Butter and milk were added to his diet and he was given 30 c.cm. of cod-liver oil daily. There was a very rapid cure of his xerophthalmia without any immediate increase in weight or height. The extra diet was continued for 10 months while he was kept closely under observation, and the increase in weight and size was not greater than that expected in a normal boy of his age.

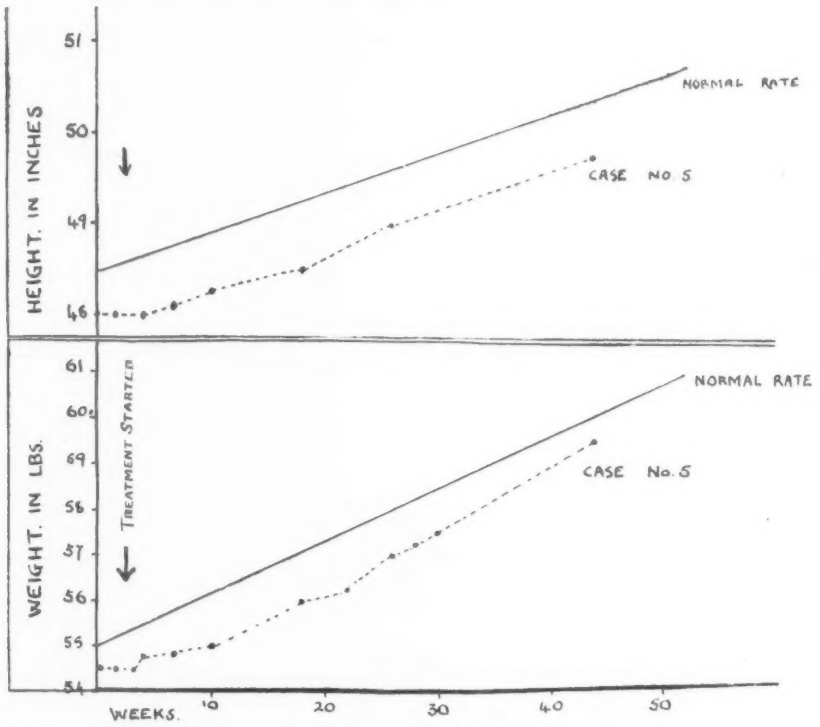

FIG. 3. Height and weight charts during treatment with cod liver oil, butter and milk. Boy of 8, with symptoms of xerophthalmia for 9 months. Had been on deficient diet for at least 2 years.

The following is another example of a boy showing rapid cure of his xerophthalmia without any increase in the rate of growth :—

A boy aged 11. The third member of a family of 7 children living in 2 rooms. Father out of work for 3 years. Total weekly income 32 shillings, with 17 shillings spent on rent, insurance, coal and clothing club, leaving 15 shillings for food. The diet was a typically deficient diet and had been so for at least 2 years. Boy attended hospital on account of night-blindness. Typical Bitot's spots on scleral conjunctiva. On Sept. 25th, 1929, weight 51 lb., height 50 inches. He was then treated with 60 c.cm. of cod-liver oil daily and extra butter in the diet. There was a rapid improvement in the night-blindness and complete disappearance of Bitot's spots in 4 weeks. The cod-liver oil and butter were continued for 6 months, when (on March 5th, 1930,) the weight was 56 lb., height 50 inches. He gained 5 lb. in weight without increase in height.

These results show that it is possible to have a form of diet deficiency which will produce xerophthalmia without affecting the general health or growth of the patient.

Relation of xerophthalmia to rickets and other deficiency diseases.—All cases under the age of 12 were carefully examined clinically and radiographically for signs of rickets, both before and after treatment. In no case was there any evidence of active rickets. In three cases aged $2\frac{1}{2}$, 4 and 12, blood-calcium and phosphorus estimations were also done. The results fell within normal limits and were not altered by treatment and the cure of the xerophthalmia. The values found are given in Table 2.

There were no signs of scurvy, beri-beri, pellagra or œdema in any case. This absence of other deficiency diseases has been confirmed by the recent observations of Weech[6], and reveals the truly specific character of the diet deficiency causing xerophthalmia.

TABLE 2.

BLOOD ANALYSES IN THREE CASES OF XEROPHTHALMIA.

Case No.	Age years	Date	Serum calcium mgrm. per 100 c.cm.	Plasma phosphorus mgrm. per 100 c.cm.
2	$2\frac{1}{2}$	14/8/29	9·6	4·0
		11/9/29	9·8	3·8
4	4	12/6/29	10·2	2·7
—	12	18/6/30	10·0	2·8
		2/7/30	9·7	2·6

Relation of xerophthalmic diet and resistance to infection.—It has been claimed by Mellanby[7] and others that vitamin A has a preventive effect against and curative influence on general infections, especially of the streptococcal group.

With this in view an investigation of the general health and incidence of disease in the families of the 11 youngest patients was carried out. All these families were fairly large, and the total number of parents and children was 99. All of these had eaten approximately the same type of diet. Over a period of two years the only serious febrile illnesses in these families were one case of pneumonia in a girl of 14 who died, two cases of mumps and three of measles with complete recovery. This does not constitute an excessive incidence of infectious disease in a group of people living on a xerophthalmia, producing diet. There was, however, a very high incidence of skin sepsis, impetigo and boils. Of the 11 xerophthalmic children 7 had a history of indolent skin sepsis which was cured remarkably quickly by anti-xerophthalmic treatment.

It is now known from the results of the pathological researches of Wolbach and Howe[8] and Tyson and Smith[9] that the most characteristic tissue change

which results from vitamin A deficiency is to be found in epithelial structures. This is a hyperplasia and then a metaplasia of cuboidal or columnar epithelium which goes on to keratinization, especially in the renal tract, air passages and salivary glands. No doubt the tendency to skin sepsis in xerophthalmia is connected with this, and is an expression of this alteration which takes place in epithelial tissues. In my cases there was other clinical evidence confirming this, namely the number of epithelial cells in the urine. I am fully aware of the apparently fortuitous manner in which bladder and renal pelvis cells may appear in the urine under various conditions, and without there being any deficiency in the diet. But in the cases severely affected with xerophthalmia the number of epithelial cells and their persistence until treatment was given was most striking. In two cases who had night-blindness alone, without xerophthalmia, there were only a scanty number which could not be regarded as abnormal. This skin sepsis and epithelium shedding into the urine must be regarded as a result of xerophthalmia-producing diet deficiency, for they both reacted to treatment with xerophthalmia-curing substances such as butter and cod-liver oil.

Results of treatment.

Some of the cases were chosen for a preliminary study of the maximum rate of cure by adding large amounts of cod-liver oil, butter and milk to the diet, so that they might be used for a basis of comparison in the trial of other forms of treatment. The first two cases were admitted to hospital for this, but it was found that although they were at first kept for a preliminary period on an experimental diet of skimmed milk, bread, margarine and jam, a rapid cure took place. It was apparently difficult to prevent a cure of the xerophthalmia as soon as any alteration from their original diet was made, even although it was attempted to keep it free from vitamin-A. It was then decided to treat subsequent cases as out-patients without revealing to them that their eye symptoms were due to a diet deficiency. In this way they continued to eat at home the same deficient diet as before, with extras which were provided for them. Thus it was possible to try the effect of such substances as ergosterol and liver extract, and of exposure to ultra-violet light, while the existing standard conditions of diet and habits were maintained.

In those cases treated with large amounts of cod-liver oil, butter and milk, the stages of cure were well defined. The first change was an improvement in the night-blindness. This was noted on the third to fifth days, and in from 7 to 14 days the vision was apparently normal. In the case of the children this could be judged by the readiness with which they returned to play with their companions in the streets at dusk. Towards the end of the first week the Bitot's spots on the scleral conjunctiva began to become more fragmented and to decrease in size, and in the severest cases had disappeared completely by the fifth or sixth week. After the disappearance of the spots some xerosis of the conjunctiva giving a characteristic lustreless appearance remained for a further 10 to 15 days. In all cases which were given adequate treatment all signs and symptoms had disappeared within two months. From this it was

accepted as a standard rate of cure that night-blindness would begin to improve within a week, and that a disappearance of the Bitot's spots would commence within two weeks, and that all signs would have disappeared within two months.

One case was treated by the addition of only 15 c.cm. of cod-liver oil daily to his diet, and another of 10 c.cm. daily. In both of these there was definite improvement of the night-blindness within a week, and complete disappearance of it within three weeks. The rate of cure of the xerosis was almost as rapid as in those cases treated with large amounts of cod-liver oil and butter.

In two cases irradiated ergosterol (radiostol) was used as treatment without any alteration in the diet. In one case 4 tablets a day were given, in the other case 12 tablets. The treatment was continued for three weeks without any improvement in the night-blindness. Thus it was judged to have no anti-xerophthalmic effect. There was, however, one result of this treatment with irradiated ergosterol which deserves mention. That was the complete and rapid disappearance of weakness and lassitude which is so frequently present in this type of diet deficiency. One of the patients, a young adult of 21, was an excellent witness and he volunteered the statement of feeling a remarkable improvement in his strength with complete disappearance of lassitude within two weeks, although there was no improvement in his night-blindness or xerosis conjunctivæ.

One case was treated with dried liver extract, effective in pernicious anæmia. He was a boy of 12 who had had intermittent night-blindness for two years. He had attended a doctor who prescribed eye lotions without giving advice on his diet. Weight 72 lb. and height 56 inches. There was a definite xerosis with Bitot's patches in all four quadrants of the scleral conjunctiva. He was given liver extract for three weeks equivalent to $\frac{1}{2}$ lb. of fresh liver a day. There was no improvement for two weeks. In the third week the boy stated he could see a little better at night, but the mother stated she did not think he had improved as he still stumbled over the chairs in the dusk, and had not yet joined the other children in their games in the streets. The xerosis and Bitot's spots were unchanged. It was judged that this pernicious-anæmia-curing liver extract had no anti-xerophthalmic effect.

One case was treated by daily exposure to mercury-vapour-lamp irradiation for four weeks, without any alteration in the diet. This had no curative effect.

Summary.

My investigation shows that nutritional night-blindness and xerophthalmia occurs sporadically in an urban industrial population, but that although large numbers of people are apparently living on the same type of deficient diet, it is only a few that become affected by the disease.

The disease was found to occur even in children whose general condition and rate of growth had been well maintained; and cure of the disease by a high vitamin diet did not necessarily result in a coincident rise in weight or height.

There was no evidence of rickets or other deficiency diseases in the affected cases.

There was a high incidence of skin sepsis amongst the cases. In the active stage of the disease there are large numbers of epithelial cells in the urine. This is a clinical confirmation of Wolbach and Howe's pathological discovery that the most specific tissue change in vitamin-A deficiency is a debasement and damage of epithelial structures.

Apart from this skin sepsis there was no evidence of a lowered resistance to general infections in people living on a xerophthalmia-producing diet.

A maximum rate of cure was studied. Using this as a basis it was shown that irradiated ergosterol, ultra-violet irradiation and pernicious-anæmia-curing liver extract have no curative effect on xerophthalmia, and that cases of xerophthalmia can be cured by adding as little as 10 c.cm. of cod-liver oil to the diet daily.

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OBSERVATIONS ON THE CHLORIDE METABOLISM IN CONGENITAL PYLORIC STENOSIS

BY

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A fall in the chlorine content of the blood in cases of high intestinal obstruction is a well-recognized biochemical finding. The opinion is generally held that the diminution in the level of the blood chlorine is due primarily to the loss of chlorine by the vomitus. Accompanying this decrease in chlorine there is an increase in the CO_2 content, resulting in a non-gaseous alkalosis with a diminution in the respiratory exchange. This increase in CO_2 would appear to be the result of the body's effort to maintain the ionic concentration of the blood at the normal level, and simultaneously, to compensate the deficiency in the acid radicle. Very strong experimental proof has been brought forward by Gamble[1] and others in favour of the truth of this hypothesis.

In a previous communication[2] we have shown that the blood chlorine tends to be low in congenital pyloric stenosis, the diminution being roughly related to the severity of the vomiting. But we have seen cases in which there was present a typical picture of alkalosis, as indicated by the raised blood CO_2 content and the depressed breathing, either during a period in which no vomiting occurred or, as in one instance, when there was a complete absence of vomiting. In Table 1 examples are given in which the depressed breathing was a feature despite the comparatively normal value for the blood chlorine. Incidentally, it shows that there is not necessarily a correlation between the

TABLE 1.

SHOWING THE BLOOD CHLORINE VALUES IN CASES OF PYLORIC STENOSIS WITH DEPRESSED BREATHING.

Name	Blood chlorides		Blood CO_2		Rate of breathing	Degree of vomiting	Urinary chloride
	mgrm. %	c.cm. N/10 %	Vol. %	c.cm. N/10 %			
T.C.	260	73·2	100·8	45·0	20 apn. +	+++	nil
J.J.	260	73·2	98·8	44·1	24 ,,	occas.	haze
J.B.	320	90·1	—	—	25 ,,	++	+
R.S.	260	73·2	107·0	47·7	21 ,,	nil	nil
	320	90·1	102·4	45·7	20 ,,	v. occas.	nil

increase in CO_2 and the decrease in chlorine. Further, in our experience the raising of the blood chlorine to normal by the administration of saline, either intra-venously or otherwise, has never resulted in a definite fall in the CO_2 content or a restoration of the breathing to normal. The last case (R.S.) is an example of the statement made above that an increase of CO_2 and decrease of chlorine may occur during a prolonged absence of vomiting. Another point of interest is the absence of urinary chlorine despite a value for blood chlorine within normal limits. These instances, it must be admitted, are exceptions to the general findings of diminished chlorine accompanying symptoms. Nevertheless, several facts emerge which make one hesitate to assume that the findings in experimental intestinal obstruction hold good for pyloric stenosis in infancy.

Despite these findings of normal blood chlorine in a certain number of cases, we are convinced that the chlorine metabolism is definitely disturbed in congenital pyloric stenosis. We have published figures[2] indicating that a very marked retention of chlorine takes place in this condition after parenteral administration of NaCl, the retention greatly exceeding that which occurs in the normal infant as well as in infants who suffer from vomiting and depletion from any other cause. In general, it may be said that in pyloric stenosis never more than 20 per cent. of the amount injected leaves the body by the urine. It may be urged that this is due to the excessive excretion and loss of chlorine in the vomitus. In several instances, however, we have been fortunate enough to have had the opportunity of estimating the urinary chlorine excretion during periods when vomiting has been reduced to a minimum or even absent. These results are recorded in Table 2. It is remarkable that the greatest retention occurred when the vomiting was least (J.D. and R.M.).

TABLE 2.

SHOWING THE PERCENTAGE RETENTION OF CHLORINE DURING PERIODS OF MILD VOMITING OR ABSENCE OF VOMITING.

Name	Date	Amount of NaCl injected grm.	Volume of urine	NaCl excreted		Percentage retention Cl	Number of vomits
				Per cent.	Total		
J.D.1	24. 5.29		220	0·059	0·130		1
	25. 5.29	1·08	170	0·105	0·179	95·4	0
2	3. 9.29		800	0·012	0·096		0
	4. 9.29	0·99	536	0·023	0·123	97·3	0
J.R.	27. 4.29		265	0·048	0·128		2
	28. 4.29	0·54	335	0·070	0·232	80·7	1
C.C.	17. 3.29		232	0·0	0·0		0
	18. 3.29	0·99	350	0·047	0·164	83·4	2
R.M.	10.10.29	0·90	67	0·006	0·004		1
	11.10.29		129	0·059	0·076	92·0	0

In the cases of J.D. and R.M., the investigation took place after a period of four weeks during which there was comparatively little vomiting. It is also interesting to note that in the second observation on J.D., the blood

chlorine was 265 mgrm. per cent. (74·6 c.cm. N/10 per cent.) prior to the intravenous injection of saline. It is evident, therefore, that the body retains chlorine in amounts exceeding the normal whether as a result of fixation in and about the tissues or because of inability to excrete the chlorine in the normal way. Further, the presence of normal values for the blood chlorine in two of the cases make it clear that the retention of chlorine may take place even when the blood has its full complement. It has been suggested by some that the renal excretion is defective and the presence of the high blood non-protein nitrogen is adduced as evidence in favour of this view. In the first place a high blood non-protein nitrogen is by no means an invariable accompaniment of pyloric stenosis, although it is present in the most serious cases, whereas a disturbance in the chlorine metabolism, so far as we have observed, is a constant accompaniment of the condition. Also, we have on several occasions estimated the urea output and have found in all a normal percentage and total output of urea. In a few cases the retention of fixed base was determined after the injection of normal saline (Table 3).

TABLE 3.

COMPARING RETENTION OF CHLORINE AND FIXED BASE IN CASES WITH AND WITHOUT PYLORIC STENOSIS.

Name	NaCl injected (c.cm. N/10)	NaCl retained (c.cm. N/10)		Fixed base retained (c.cm. N/10)		Remarks
		Actual	% of extra intake	Actual	% of extra intake	
J.R.	92·3	74·3	80·7	45·6	49·4	Pyl. stenosis
C.C.	169·0	141·0	83·4	67·0	40·0	,, ,, (before op.)
,,	154·0	1·0	0·6	28·9	18·7	,, ,, (after op.)
B.W.	154·9	22·0	13·3	50·7	33·0	No pyl. stenosis

It is seen that the pyloric cases showed a much lower retention of the extra base than of the extra chlorine, whereas after operation and in the feeding case the reverse occurred. It would seem, therefore, that in pyloric stenosis there is a preferential retention of chlorine over fixed base, and that the reverse holds good in the non-pyloric cases.

Gamble and Ross[1] have shown that in dogs with experimental occlusion of the pylorus there is a deficiency both of fixed base and chlorine, the latter being the more marked because of the presence of HCl in addition to the BCl in the vomitus. This explanation is not wholly satisfactory as in the cases detailed vomiting was very slight. Further, we have never been able to demonstrate the presence of free HCl in the stomach contents. Neutral chlorides, however, were always present. We would therefore suggest that the chlorine is retained in the body, partially at any rate, in a form other than BCl.

Rominger and his co-workers[3] have shown that in the normal infant more sodium than chlorine is retained after the administration of NaCl. These

same observers have also pointed out that chlorine may be retained apart from water—in other words, a dry retention of chlorine. In view of these findings with urea and fixed base it appears improbable that defective renal excretion provides an adequate explanation for the high retention of chlorine after parenteral administration of NaCl.

These observations on the retention of chlorine led us to investigate the possibility of the existence of a partial chlorine vacuum in the tissues in the fatal cases. Considering the importance of chlorine to the body economy, remarkably few investigations appear in the literature as to the variation in the content of the tissues. Von Noorden[4] gives 0·188 per cent. Cl (52·9 c.cm. N/10) as the average of the bodies of new-born infants, the extreme values being 0·138 per cent. and 0·194 per cent. Analyses of individual tissues in the human subject are rare. Observations have, however, been made on adult tissues by Katz[5], Moraczewski[6] and Hutchison[7] who report figures varying from 0·070 per cent. (19·7 c.cm. N/10) in muscle to 0·219 per cent. (61·7 c.cm. N/10) chlorine in lung. Since no figures pertaining to individual tissues of infants could be found, it was considered advisable to obtain normal standards for the chlorine content of the various tissues as well as to determine the chlorine content of the tissues in the fatal cases of pyloric stenosis. One appreciates, of course, that actually no truly normal tissues can be had, but from the post-mortem material of those cases in which there was no reason to suspect any such change as has been observed in pyloric stenosis, we obtained samples of various tissues. In all, tissues from six cases were analysed (Table 4).

TABLE 4.

SHOWING THE CHLORINE CONTENT OF THE VARIOUS TISSUES OF THE INFANT, EXPRESSED IN C.CM. N/10.

Group	A			B			C		
Tissue	Normal cases (six)			Pylorics to whom no saline has been given (4 cases)			Pylorics to whom saline had been given (4 cases)		
	Max.	Min.	Aver.	Max.	Min.	Aver.	Max.	Min.	Aver.
Muscle	54·5	38·2	43·2	31·5	20·0	24·6	69·8	46·0	60·9
Liver ..	45·9	25·6	36·5	30·3	17·8	23·0	67·6	32·5	50·6
Lung ..	62·5	47·5	52·4	38·6	19·1	30·7	84·8	37·6	56·6
Heart ..	41·9	32·7	37·7	16·8	16·5	16·7	48·6	22·2	32·2
Kidney	44·8	39·8	42·1	29·2	15·9	23·0	73·2	29·0	49·2
Brain ..	58·5	35·9	48·9	41·5	8·2	24·9	62·8	39·7	48·9
Skin ..	47·7	32·5	39·2	25·2	19·1	24·5	65·4	39·4	56·3

The method used in estimating the chlorine content of the tissues was the one elaborated by Van Slyke[8]. Portions of the various organs were obtained at the time of the post-mortem examination, and in each case were minced, mixed and weighed as soon as possible. All determinations were done in

duplicate because of the possibility of error due to the unequal distribution of the tissue juices throughout the organ. Duplicates were consistent in all cases, the error never exceeding 10 per cent. and usually being much less. In Table 4, the results of the analysis of six such normal cases are shown (Group A) as well as the figures for the analysis of the tissues of eight fatal cases of pyloric stenosis in four of whom saline had been given (Group C) and four where no such treatment had been adopted (Group B). To conserve space, only the maximum, minimum and average figures have been quoted. One case, P.T. (Case 3), is not included in any group, since this infant, although not receiving any saline, had a very extensive broncho-pneumonia accompanied by a marked œdema.

The individual values of the various tissues in the cases of Groups B and C are given in Tables 5 and 6.

TABLE 5.

SHOWING THE CHLORINE CONTENT (NaCl C.CM. N/10%) OF THE VARIOUS TISSUES OF OF FOUR FATAL CASES OF PYLORIC STENOSIS TO WHOM NO SALINE HAD BEEN GIVEN.

Name	Muscle	Liver	Lung	Heart	Kidney	Brain	Skin
W.F. ..	21·6	22·6	—	16·5	20·7	8·2	25·2
A.S. ..	25·4	21·2	34·4	—	29·2	—	19·1
J.L. ..	20·0	17·8	19·1	—	15·9	—	19·2
J.R. ..	31·5	30·3	38·6	16·8	26·3	41·5	—

TABLE 6.

SHOWING THE CHLORINE CONTENT (NaCl C.CM. N/10%) OF THE TISSUES OF FOUR FATAL CASES OF PYLORIC STENOSIS TO WHOM SALINE HAD BEEN GIVEN.

Name	Muscle	Liver	Lung	Heart	Kidney	Brain	Skin
T.C. ..	—	32·5	37·6	22·2	29·0	39·7	39·4
J.J. ..	46·0	42·2	47·5	25·7	40·5	42·4	50·2
J.B. ..	67·1	60·2	—	48·6	54·1	50·7	65·4
R.S. ..	69·8	67·6	84·8	—	73·2	62·8	60·0

It will be noted that in those cases not receiving saline the chlorine content is very greatly diminished, the maximal values of this group being usually below the minimal in the normals. These results point very convincingly to the existence of a diminished chlorine content of the tissues in cases of pyloric stenosis. Of the four cases of the last group, all of whom had been given saline, the route being intra-venous or intra-peritoneal or both, with the exception of one case in which the saline was given by mouth, high values were obtained, the average for this series exceeding the averages obtained for the control group. It must therefore be concluded that the administration of saline is capable of raising the diminished tissue chlorine content to normal or even to values above normal.

In three patients œdema occurred during the course of the disease; in two the œdema seemed to be related to the administration of the saline but in the third case, P.T. (Case 3), previously mentioned as not having been included in any group, no saline had been given. Administration of saline in similar amounts to healthy infants or to those suffering from gastro-enteritis rarely leads to the production of œdema, although a sudden rise in weight presumably due to a retention of water may occur. The anomaly of the presence in excess of a fluid rich in chlorine in the pericellular spaces during a condition which is characterized by chlorine impoverishment seems worthy of comment and investigation. The significant details of these three cases are therefore discussed.

Case 1.—J.B., a male infant aged six weeks had been vomiting since one week of age. He was a small emaciated infant weighing 4 lb. 13 oz. Visible gastric peristalsis was present and a pyloric tymour was palpable. The breathing was shallow with definite apnœic periods. The rate was 25 per minute.

The progress of the case and the associated blood findings were as follows:—

13.11.29.—Admitted to ward. The blood examination revealed the following:—Total CO_2 content: 83 vol. per cent. (28·0 c.cm. N/10 per cent.). Chlorides: 225 mgrm. per cent. (63·3 c.cm. N/10 per cent.). Non-protein nitrogen: 68 mgrm. per cent. The urine contained no chlorine. 100 c.cm. normal saline injected intra-venously.

14.11.29.—Feet puffy. 100 c.cm. normal saline injected intra-venously.

15.11.29.—Definite œdema present. 100 c.cm. normal saline injected intra-venously.

16.11.29.—Blood chlorine: 320 mgrm. per cent. (90·1 c.cm. N/10 per cent.). Œdema more marked. Breathing still shallow.

19.11.29.—Œdema still present but much less than on 16th.

20.11.29.—No œdema. Blood chlorine: 320 mgrm. per cent. (90·1 c.cm. N/10 per cent.). 100 c.cm. normal saline injected intra-venously. Infant died.

At the commencement of the treatment, it seems safe to assume on the strength of the low blood chlorine content that there was a depletion of the chlorine content of the tissues. The first injection of normal saline led to a retention of 90·9 per cent. of the amount injected and simultaneously to the development of œdema. After 24 hours there was puffiness of the feet and the next day after the second injection, definite pitting on pressure. The ensuing injections of saline led to retentions of 86·8 per cent. and 56·3 per cent. respectively. In all, 2·7 grm. were injected and only 0·54 grm. excreted, *i.e.*, a retention of 78 per cent. Yet this took place during the onset and definite increase of œdema. During this period there was an increase in weight of 206 grm., which approximates the weight of saline retained on the assumption that the NaCl was retained in a 0·9 per cent. solution. Thus, the weight of saline injected was roughly 300 grm., the weight of normal saline excreted was 66 grm., leaving 234 grm. retained. The urinary output of chlorine gradually increased to the period ending November 16th and was followed by a rapid decline accompanied by a diminution of the œdema. On 19th, the weight was 57 grm. above that on 12th, while the total amount of intra-venously administered saline not lost in the urine was 1·49 grm. ,corresponding to 167 grm. of 0·9 per cent. NaCl solution. Two possibilities as to the reason for this discrepancy offer themselves. Either the retention of NaCl might have been only apparent, the loss taking place through the vomitus

or the chlorine might have been stored apart from water. It was unfortunately impossible to collect the vomitus accurately, but on one day during which the vomiting was the most marked of the period an attempt was made and the collection yielded 200 mgrm. of NaCl. As it was believed that approximately only half the vomitus was obtained, this would mean a loss by the vomiting of 400 mgrm. daily and for the six day period, 2·4 grm. whereas the amount not excreted by the urine over the same period was 1·5 grm. It is possible therefore that the extra chlorine was lost in the vomiting. However, the tissues were found to have a very high value for chlorine, varying from 0·266 per cent. (67·1 c.cm. N/10 per cent.) in heart muscle to 0·172 per cent. (48·6 c.cm. N/10 per cent.) in lung. With the exception of the brain all were above the maximum values for the control series. The saline given prior to the death of the infant contained 0·9 grm. NaCl (15·4 c.cm. N/10 per cent.) which could not possibly have raised the chlorine content of the tissues to such an extent.

In any case, whatever the amount lost by the vomiting, this infant stored chlorine in the tissues to a degree far exceeding the normal. That the storage of chlorine had taken place prior to the last injection of saline is indicated by the high normal blood chloride value (320 mgrm. per cent., 90·1 c.cm. N/10 per cent.) previous to the last injection.

This case also raises the question of why the urinary output of chlorine was so low in the presence of œdema. Evidence of impairment of renal function could not be obtained. The defect in metabolism would appear to be in the tissues themselves. The picture presented resembles that seen in 'nephrosis' where the chlorine appears in minimal quantities in the urine although the power of excreting nitrogenous substances seems quite unimpaired. The first injection of saline would, owing to the depletion of the tissue chlorine lead to an outpouring of chlorine from the blood to the tissue. This outpouring would, however, go beyond the equilibrium point, a state of affairs that is well known in in vitro experiments, and which would take some time to adjust itself. Next day, in spite of the now partially replete tissue chlorine, the intra-venous injection of more saline, by suddenly raising the blood chlorine would again lead to the passage of chlorine to the tissues beyond the equilibrium point. The third injection would still further increase the amount of chlorine in the tissues. Forty-eight hours after the last injection of saline, the œdema commenced to disappear but without the simultaneous excretion of chlorine by the urine. Some of the chlorine was lost in the vomitus and some was retained in the tissues as revealed by the post-mortem analysis. Whatever the proportion retained, one is forced to the conclusion that the chlorine was present either in the tissues or the blood, or both, in a form which can only be excreted with difficulty by the kidney. The fact that prior to the injection of saline the blood chlorine content was 320 mgrm. per cent. (90·1 c.cm. N/10 per cent.) while the urinary chlorine was fractional in amount would suggest that the fault is either in the blood or the kidney.

It should also be mentioned that although the chlorine content of the blood on November 16th was slightly above normal the shallow breathing persisted. Unfortunately the CO_2 was not estimated, but the presence of the

depressed breathing is sufficient to raise doubt regarding the diminution of the blood chlorine being the sole factor in the production of the alkalosis. One might suggest that part of the chlorine was not united to base, thereby leaving an excessive amount of the latter to unite with CO_2. It seems to us that only by assuming that a portion of the chlorine is not united to base can one explain, first, the depressed breathing accompanied by a high CO_2, and secondly, the fact that chlorine does not appear in the urine although the body seems to have its full quota. The urinary findings in this case are given in Table 7.

TABLE 7.

SHOWING THE URINARY FINDINGS IN CASE 1 (J.B.) AND THE PERCENTAGE RETENTION OF NaCl AFTER INTRA-VENOUS INJECTION OF NORMAL SALINE.

Date (Nov. 1929)	Volume of urine	Urinary NaCl %	Urinary NaCl total	NaCl injected intra-ven. grm.	Percentage retention of NaCl
12—13	82	nil	nil	—	—
13—14	100	0·0819	0·0819	0·9	90·9
14—15	91	0·1304	0·1187	0·9	86·8
15—16	105	0·3744	0·3931	0·9	56·3
16—17	93	0·3159	0·2937	—	—
17—18	71	0·2457	0·1743	—	—
18—19	60	0·2340	0·1404	—	—
19—20	39	0·3276	0·1278	—	—
20—20	59	0·5850	0·3452	0·9	75·8

Case 2.—R.M., a male infant came under observation at the age of six weeks with a history of expulsive vomiting since two weeks of age. Gastric peristalsis was visible and a pyloric tumour readily palpable. The breathing was depressed with apnœic periods.

On admission the blood findings were as follows:—

Total CO_2 content: 114·8 vol. per cent. (51·2 c.cm. N/10 per cent.). Chlorine content: 190 mgrm. per cent. (53·5 c.cm. N/10 per cent.). Non-protein nitrogen: 57·6 mgrm. per cent.

The injection of 50 c.cm. normal saline led to an increased output of chlorine in the urine equivalent, however, to only 2·7 per cent. of the extra intake. A week later, four daily intra-venous injections of saline were given. Just before the commencement of this treatment the blood examination yielded the following figures:—

Total CO_2 content: 121·6 vol. per cent. (54·3 c.cm. N/10 per cent.). Chlorine content: 230 mgrm. per cent. (64·8 c.cm. N/10 per cent.). Non-protein nitrogen: 57·6 mgrm. per cent.. and between the third and fourth injections the findings were:—

Total CO_2 content: 69·6 vol. per cent. (31·0 c.cm. N/10 per cent.). Chlorine content: 270 mgrm. per cent. (76·0 c.cm. N/10 per cent.). Non-protein nitrogen: 32 mgrm. per cent.

The output of chlorine was very low, averaging only 0·048 grm. per day over a period of ten days, and there was a rapid rise in weight which was associated with the presence of considerable œdema (pitting on pressure). The vomiting was fairly severe but apparently not sufficient to get rid of the chlorine in the œdematous fluid. Despite the almost normal chlorine content of the blood on the second last day, the amount of NaCl excreted was only 0·062 grm. About a month later the blood chlorine was 305 mgrm. per cent. (86·0 c.cm. N/10 per cent.) and the daily output in the urine only amounted

to 0·004 grm. and given after the injection of 100 c.cm. of normal saline, this was only increased to 0·076 grm. although vomiting only occurred once. This infant made an uninterrupted recovery without operation and on dismissal was excreting as much as 1·0 grm. NaCl daily. It would therefore seem that during the active stage of pyloric stenosis the chlorine is present in some form that cannot be excreted by the kidney.

Case 3.—P.T., a male infant thirteen weeks of age came under observation because of vomiting which had begun at one month of age. Visible gastric peristalsis seen and a pyloric tumour palpable. The infant was acutely ill on admission with a broncho-pneumonia involving both lungs. On admission, Dec. 23rd, 1929, the blood analysis yielded the following figures :—

Total CO_2 content : 95·4 vol. per cent. (42·6 c.cm. N/10 per cent.). Chlorine content : 230 mgrm. per cent. (64·8 c.cm. N/10 per cent.). Non-protein nitrogen : 68·2 mgrm. per cent.

The vomiting was marked on the two following days but slight on Dec. 25th. On the 26th there was an increase in weight of 115 grm. and on the 27th of 145 grm. Simultaneously with this increase in weight, the vomiting ceased and did not recur. On the 27th slight œdema of the feet was noticed. This œdema gradually increased and before death there was well-marked œdema of both feet and lumbar region. Analysis of the tissues revealed the chlorine content of the tissues to be within normal limits.

This case illustrates the development of œdema without the parenteral introduction of saline. It is possible that the pneumonic condition as such led to the œdema. In lobar pneumonia, a retention of chlorine with increase in weight is a well-recognized phenomenon. The broncho-pneumonia involved all lobes of the right lung and the lower lobe of the left lung while the upper lobe was the seat of acute emphysema. It may be that the extensive consolidation rendered difficult the escape of CO_2 which accordingly would be retained and probably displace the chlorine. The chlorine would be either passed to the tissues or lost by the vomit in order to make room for the excess CO_2. It will, however, have been noted that the rise in weight dates from the cessation of the vomiting and in view of these facts it is suggested that the chlorine from the BCl of the blood is shunted to the tissue spaces. Once in the tissue spaces, despite the gradual repletion of the tissue chlorine, the base chlorine cannot get back into the blood stream in sufficient amount to be excreted by the kidney owing to the fact that the CO_2 is holding up the base. Here again it is necessary to postulate either a renal defect or the presence of the chlorine in a form which cannot be dealt with by the kidneys.

The following case is briefly discussed because it lends additional support to the theory that the chlorine is present in a form other than BCl.

Case 4.—R.S., a female infant, came under observation at the age of 8 weeks. Vomiting had begun at the age of 3 weeks. Visible gastric peristalsis was present and a pyloric tumour palpable. The blood examination at this time was as follows :—

Total CO_2 content : 152·0 vol. per cent. (67·9 c.cm. N/10 per cent.). Chlorine content : 200 mgrm. per cent. (56·3 c.cm. N/10 per cent.). Non-protein nitrogen : 57·1 mgrm. per cent.

During the first fortnight in hospital the infant was given frequent intra-venous and intra-peritoneal injections of normal saline as well as saline by the mouth, and although vomiting was frequent no œdema was noted. The rise in weight following each injection was only temporary lasting usually not longer than one day. The blood chlorine, however, did increase and this was accompanied by a fall in the total CO_2 content. Three weeks after admission the blood was as follows :—

Total CO_2 content : 65·3 vol. per cent. (29·1 c.cm. N/10 per cent. Chlorine content : 305 mgrm. per cent. (86·0 c.cm. N/10 per cent.). Non-protein nitrogen : 65 mgrm. per cent.

Before the death of the infant the value for the blood chlorine was 380 mgrm. per cent. (107·0 c.cm. N/10 per cent.) an amount definitely in excess of normal. Although the chlorine content of the blood was more than replete, the breathing remained depressed. The analysis of the tissues for chlorine revealed very high values. It is difficult to understand how the great retention of chlorine took place without any signs of obvious œdema if the retention was in the form of inorganic chlorine. The urine was examined on several occasions and even when the blood chlorine content was high, it only contained a trace of chlorine. This finding by itself would lead to the conclusion that the chlorine must have been in great part present in a form other than BCl. The association of these various phenomena, namely the high chlorine content of the blood and tissues with no œdema, and the absence of more than a trace of chlorine in the urine seems to lead to no other conclusion.

Summary.

The observations recorded in the foregoing pages appear to justify the following conclusions :—

1. In untreated pyloric stenosis there is a partial chlorine vacuum in the tissues. This can be corrected by the administration of saline which, if continued, frequently leads to an excessive retention of chlorine and the production of œdema, even when the chlorine content of the blood is normal. In such cases the chlorine content of the tissues is higher than normal.

2. Restoration of the blood chlorine content to normal does not result in a correction of the alkalosis as is evidenced by the persistence of the high total CO_2 content and the depressed breathing.

3. A normal blood chlorine content may be accompanied by a fractional amount of chlorine in the urine.

4. To permit of a satisfactory explanation of these findings, it appears necessary to postulate either (1) the inability of the kidney to excrete chlorine : or (2) more probably, in view of the findings with urea and fixed base, the presence of chlorine in the tissues in a form other than BCl. Certain evidence is brought forward in support of the latter view.

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PNEUMONIA IN MEASLES

BY

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The steady decline in the virulence of diphtheria and scarlet fever which has been in progress during the present century has thrown into sharper prominence the continued severity and fatality of measles.

Taking epidemic and non-epidemic years together, measles is responsible for 0·8 per cent. of deaths from all causes in this country, and must be held responsible for much chronic ill-health, as a result of its pulmonary complications. In average epidemics all but a negligible proportion of the deaths occur within the first five years of life in communities in which measles is endemic.

Cause of death in measles.—On the average about four-fifths of measles deaths are directly attributable to pneumonia in one form or another, broncho-pneumonia of a severe type being responsible, as is well known, for the greatest number.

During the 1927–28 epidemic, 86 per cent. of deaths occurring from measles in Metropolitan fever hospitals were due to pneumonia. From 1916–1927 inclusive, measles appears as a cause of death in the Grove Hospital register in 193 cases. The immediate cause of death is given as broncho-pneumonia in 153 cases (80 per cent.), lobar pneumonia 6 cases (3 per cent.), and other miscellaneous causes in 34 cases (17 per cent.). On the whole, when large numbers are considered, the case mortality in England has not fluctuated very much over a number of years, though the segregation of severe cases in various institutions has at times been productive of tables of statistics which are by no means representative of normal conditions.

Treatment of measles in hospitals.—The case mortality among cases treated in hospitals appears to be so gravely in excess of that observed in those which are left at home, that the argument is sometimes advanced that no attempt should be made to accumulate cases of measles in large institutions, on account of the dangerous infectivity of measles pneumonia under the over-crowded conditions which are likely to exist in hospital wards during epidemics (Sowden[26]). The L.C.C. fever hospital statistics (1927–28) do not, however, support this contention. The case mortality among those children who were admitted to hospital suffering from pneumonia was 31·7 per cent., while among those who were free from pneumonia on admission it was only 1·9 per cent. There is no consensus of opinion as to whether or no pneumonia in measles should be regarded as dangerously infective, but in this country it is not usually so regarded, and no attempt is made as a rule to segregate cases with

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pneumonia from the rest. On the other hand the late C. B. Ker wrote in his well-known text-book of infectious diseases, 'I have no doubt the condition may be infectious from patient to patient,' but he supplied no information on the frequency of such infection. French writers appear to be unanimously of the opinion that measles pneumonia is highly infectious, and Hallé[9] has stated that every case of measles should be strictly isolated.

During the 1927–28 epidemic an opportunity occurred at the Grove Hospital of studying the effect of nursing measles cases in isolation. The cubicles which were used consisted of glass partitions, seven feet in height, within the main body of the ward, access being afforded by a central corridor. Isolation was, therefore, not absolute, since the patients breathed a common atmosphere, although a spray infection could be practically excluded. The results were :—

Jan. 1927—June 1928.	Cases.	Pneumonia deaths.	Mortality.
Cubicles	112	6	5·4%
General ward	106	5	4·7%

During the period under review the average hospital death rate from pneumonia was 5·4 per cent., the same as that of the cubicle ward. It may, I think, be concluded that measles can be safely nursed in general wards provided that the density of beds is kept within proper limits. A minimum of 144 square feet of floor space per bed should be maintained.

Previous investigations on pathology and bacteriology.

About fifty years ago Cornil and Babes, writing in the Traité de Medicine of Charcot, Bouchard, and Brissot, described a form of broncho-pneumonia which they considered might be due to the unknown virus of measles, since it did not appear to be associated with any of the micro-organisms invading the respiratory tract familiar to them. These observations were made before the discovery by Pfeiffer of the so-called hæmophilic group of bacteria. According to Cornil and Babes the essential lesion consisted of an acute inflammation of the peri-bronchial lymphatics leading to a diffuse infiltration of the inter-alveolar connective tissue. The mortality was very high, and the authors observed that in those cases which survived, the disease tended to run a prolonged course closely resembling pulmonary tuberculosis from which, in fact, it was but rarely distinguished.

Interstitial pneumonia.—The occurrence of acute interstitial pneumonia has been frequently remarked in measles.

In 1884 Delafield[4] emphasized this and pointed out that consolidation of the lung was generally due to lateral pressure on the alveoli adjacent to the bronchioles, being in fact a species of atelectasis.

Steinhaus[27], dealing with measles in children, distinguished this species from the common lobular type of broncho-pneumonia in which there is a catarrhal exudate, and noticed that the alveoli may be filled with fibrin. Hecht[10] gave a very similar account.

In 1921 MacCallum[19] in an exhaustive monograph described the types of pneumonia occurring in a large outbreak of measles among soldiers in camp. He considered that focal areas of consolidation in the lung resulted from a primary bronchiolitis and peri-bronchiolitis produced by the propagation of an inflammatory irritant by way of the lymphatics. He distinguished two varieties of inflammatory process: one, an acute focus with exudate into the alveoli, fibrin being always abundantly present in recent cases; secondly, a more chronic focus proceeding in the form of a proliferative interstitial peri-bronchitis with striking changes in the interstitial tissue but no exudate into the alveoli. This second type was prone to lead to suppuration in the lung and empyema. The organism most frequently discovered was a hæmolytic streptococcus. It must be noted that all MacCallum's patients were young adults, and that the whole epidemic spread from a single limited geographical centre, since it is principally on the strength of this epidemic that hæmolytic streptococci have been so generally considered to be the organisms most prevalent in the lungs in measles. Previously Hektoen had found hæmolytic streptococci predominating in measles in military camps, but Knowlton was doubtful of the significance of these findings. Knowlton made cultures from the throats of 458 cases of measles (mortality 2·7 per cent.), and found hæmolytic streptococci present in 122 cases. Pneumonia occurred in 10·6 per cent. of these cases. In 336 cases which were negative to hæmolytic streptococci, pneumonia occurred in 10·4 per cent. It was, however, noted that streptococci predominated in the pneumonias occurring in those patients who were previously negative to streptococci. Knowlton considered that these findings pointed to the conclusion that in many cases the primary organisms associated with measles pneumonia, tend to be replaced by hæmolytic streptococci at a later stage.

Frequency of empyema.—Empyema was a frequent occurrence in all these camp epidemics and I am inclined to believe that the frequency of empyema in measles may be regarded as in some measure an index of the prevalence of hæmolytic streptococci.

TABLE I.

COMPARATIVE FREQUENCY OF EMPYEMA IN PNEUMONIA.

	Type of case	Authors	Total cases	Empyema	Per-centage
Pneumonia not due to measles	Children with br.-pneumonia	McNeil, Macgregor and Alexander[20], 1929	140	34	24
	Children with pneumonia	Queen's Hospital for Children, Annual Report, 1927 ...	106	15	14·2
Pneumonia following measles	Adults ...	Opie, Blake, Small and Rivers[21], Camp Pike, 1921	56	9	16
	Children ...	Grove Fever Hospital, 1916—1927	232	5	2·2
	Children ...	South Western Fever Hospital, 1913—1921	161	4	2·5

It can be seen from Table 1 that there is a significant difference between the incidence of empyema in childhood when measles is the predisposing condition when compared with other forms of broncho-pneumonia. Now measles is accompanied by such severe forms of pneumonia that the relative immunity of London children to empyema is not very easy to explain. The argument that in measles there is no tendency to the formation of purulent

exudates is not supported by the observed frequency of such exudates among adults ; moreover, in all such exudates hæmolytic streptococci are found with greater frequency than any other group of organisms, pneumococci being more frequent in primary forms of broncho-pneumonia. Pneumococcal pneumonia in measles appears to result from exaltation in virulence of the normally harmless saprophytes of the nasopharynx, and these are less liable to produce purulent effusions than are type I and II pneumococci.

Further, there is some reason to suppose that very young children (i.e., those in the age groups on which falls the maximum incidence of measles pneumonia) are relatively resistant to the invasions of streptococci. The different average age incidences of measles and scarlet fever may perhaps be quoted in support of this view, as well as the fact that the majority of infants in their first year of life are Dick-negative (Zingher[33]). The occurrence of effusions in the recent epidemic (1929–1930) is interesting in this connection. From October to February severe pneumonia was prevalent but no empyemata occurred. It was also observed that during the months of December, 1929, and January and February, 1930, hæmolytic streptococci were extremely scarce from any source (e.g., cultures from the mastoid, antrum, throats, etc.). Towards the end of February the streptococci began to appear again (the last 3 or 4 cases dealt with in this investigation were streptococcal pneumonias, and date from the second half of February) : while in March four empyemata occurred, two of which were fatal, and in three of these cases the hæmolytic streptococcus was found in pure culture. In March, 1929, streptococcal empyemata were also more frequently noted than in any other month on that occasion in connection with influenza.

On the whole, I think, there are good grounds for believing that scarcity of empyema in most epidemics of measles in children, is due to the comparative rarity of streptococcal pneumonia in young children suffering from this disease.

B. influenzæ in measles.—This association has been described by various authors.

MacCallum[19] noted the association of organisms resembling the bacillus influenzæ (Pfeiffer) with streptococci in some of his cases and remarked :—' It may be that they (B. influenzæ) tend to be associated with interstitial and organizing processes, and one might leap to the conclusion that they are responsible for these processes, or even that they are the forerunners of the streptococcus and pneumococcus infection.' Alteration in the bacterial flora of the lungs as the disease progresses has been noted by various authors. In another outbreak of measles in an army camp, Opie, Blake, Small and Rivers[24] showed that pneumonia was due at the outset either to the pneumococcus alone, or to this organism associated with influenza bacillus, though certain of their cases became complicated later by a hæmolytic streptococcus. They also noted that empyema was rare in the absence of such a late infection. They considered that a common sequence of events in measles might be the same as that so frequently noted in influenza ; first bronchial infection with B. influenzæ, then pneumonia due to the pneumococcus, followed at a later stage by necrosis and suppuration produced by hæmolytic streptococci. Such a sequence was observed in one of my series (Case 46).

Four hundred and eighteen cases among soldiers in camp on Salisbury Plain were examined by Eyre and Lowe[5] who discovered streptococci in 96 per cent. and B. influenzæ in 72·5 per cent. of sputa, and in 2 cases B. influenzæ in pure culture in the lungs. The frequent appearance of B. influenzæ in the respiratory tract of patients with uncomplicated measles has been noted by Bordet[2], and especially in children by Davis[3].

Relation of measles to influenza.—Wolbach[32] described acute interstitial pneumonia as a feature of the great influenza pandemic of 1918, and obtained the B. influenzæ in pure culture from the lungs in a number of cases. In many respects measles bears a close resemblance to influenza, especially as regards the pathology and bacteriology of the complications : thus to quote Hallé[9] :—

'La flore bactérienne de ces complications (i.e., measles pneumonia) est en effet le même que celle des broncho-pneumonies grippales, en première ligne le streptocoque hæmolytique, pur, ou associé au pneumocoque, au staphylocoque, ou au pneumobacille de Friedlander. Ils sont souvent précédés à un premier stade par un cocco-bacille qu'on est bien d'homologuer avec le bacille de Pfeiffer.'

Lewis[15] discussing the occurrence of B. influenzæ in measles considered that the periods during which the wide diffusion of the influenza bacillus has been found, have always been periods following the mild missed prevalences of true influenza of respiratory type. A comparison, however, of the crude death rates from both diseases over a number of years does not point to any intimate connection between them (see Table 2), but the true significance of

TABLE 2.

DEATHS FROM MEASLES AND INFLUENZA, 1913—1923.
(ENGLAND AND WALES.)

	1913	1914	1915	1916	1917	1918	1919	1920	1921	1922	1923
Total deaths from measles ...	10,644	9,144	16,445	5,513	10,538	9,787	3,534	7,190	2,241	5,894	5,316
Total deaths from influenza ...	6,394	5,964	10,484	8,791	7,289	112,329	44,801	10,665	8,995	21,498	8,461

The M.A.B. measles case mortality of 1918 was 13·2, the highest recorded, but there does not appear to be any very clear correlation between the crude death rates. The high mortality of 1915 for measles is accounted for by outbreaks among troops in camp.

the B. influenzæ in influenza has hardly yet been decided, although after a temporary eclipse, it has undergone a certain rehabilitation[29] The matter is further complicated by the demonstration by many bacteriologists that the B influenzæ is very widely diffused among perfectly healthy people, and this fact appears to have led to the undeserved neglect until quite recently of Pfeiffer's bacillus as a dangerous pathogenic agent.

Primary acute interstitial pneumonia in children.—In a recent important series of papers McNeil, MacGregor, and Alexander[20] have noted the occurrence of acute interstitial pneumonia as a primary disease of children. They point out that the essential process is a progressive lymphangitis which begins in the peri-bronchial lymphatics, spreads down to the peri-vascular connective tissue of the lung and causes interstitial proliferation. They also observe that this mode of invasion is the reason for the severity of the disease, and for its undesirable consequences.

The general picture presented in such cases appears to be identical with that which is found in many of the most acute cases caused through measles, some of which will be described later. The acute lymphangitis in measles cases can be observed post mortem. The submucous lymphatics of the larynx and trachea are invaded in the first place, and a rapid downward spread occurs into the peri-bronchial lymphatics. There are no definite lymphatic vessels demonstrable in the parenchyma of the lungs, but a remarkable endothelial proliferation of the alveolar wall is seen to occur. Some of the alveoli are compressed by this process, while those in any portion less affected by the morbid process become notably emphysematous. Sometimes there is an effusion of fibrin into neighbouring alveoli, but polymorphonuclears are always conspicuously rare (Fig. 1–4).

Working in connection with the authors quoted above, Glen Liston made a bacteriological examination in 40 cases showing this condition, and demonstrated the presence of B. influenzæ in 33 (85 per cent.) of them using Sopakar's medium. Reviewing the evidence he concludes that B. influenzæ may be considered as the true cause of this acute form of pneumonia, to which conclusion I can bring further support. It is interesting to note that Glen Liston found the organism six times in the blood stream, once in pure culture, and five times in association with other organisms.

The general conclusion reached was that the B. influenzæ opens a path for the invasion of the respiratory tract by secondary organisms which are the cause of empyema, abscess of the lung, bronchiectasis, etc. Only one of the cases dealt with in the papers here quoted was definitely attributable to measles.

Other organisms found in the lungs in measles pneumonia.—Various secondary invaders have been described in the lungs in measles besides the hæmolytic streptococcus, but streptococcus viridans of whatever species is rarely found. The hypothesis that measles may be caused by a green-producing streptococcus, put forward by Tunnicliffe[30], Ferry and Fisher[6] and others, led Mair[21] to examine the flora of the upper respiratory tract in fifty children in the early stages of measles by allowing them to cough over rabbits-blood agar plates. In no case did any colonies of streptococcus viridans develop although this type can be cultivated with ease from the tonsils at all stages of the disease. In my series (74 cases) they developed in three cases of pneumonia in pure culture from the lungs, and from the larynx in addition in one case (No. 71) which was complicated by acute laryngitis.

As would be expected the pneumococcus has frequently been found in measles pneumonia. Members of the heterogeneous fourth group are probably present in the great majority of cases

I have not had an opportunity of determining this point in the present investigation but the findings of Glynn and Digby[7] appear conclusive These authors examined 879 cases of pneumococcal broncho-pneumonia with this result :—

Type I	...	...	17 (1·9%)
Type II	...	...	79 (9·0%)
Type III	...	...	91 (10·3%)
Type IV	...	...	692 (78·7%)

Glynn considered that the features most characteristic of a group IV infection were :—

(1) The onset is generally gradual : the symptoms pass slowly and less often suddenly into those broncho-pneumonia.
(2) The temperature is generally high but not sustained, and is usually marked by daily remissions of three degrees or more.
(3) Pyrexia ends by lysis, never by crisis.

These criteria are certainly fulfilled in a large number of cases due to measles in which pneumococci preponderate. A relative leucopenia appears to be less unfavourable in pneumococcal than in other forms of pneumonia.

Summary of previous investigations.—The evidence cited thus far has indicated that :—

(1) Acute interstitial pneumonia occurs in adults with measles (MacCallum[19], Hektoen[11]).
(2) Acute interstitial pneumonia is found as a primary disease in children (McNeil, Macgregor and Alexander[20]).
(3) B. influenzæ is frequently associated with this type of disease (Liston[17])
(4) B. influenzæ may pave the way for attacks by later invading organisms (Opie and Blake and others[21])

Present investigations.

In the present investigation the results of a bacteriological study of 75 cases of pneumonia occurring during successive epidemic waves of measles, are recorded.

These cases afford a fair average sample of the type of pneumonia occurring at any one time in the London area. In every case cultures were made directly from lung punctures, since no other method can be expected to afford trustworthy evidence of the nature of the organisms invading the bronchioles and alveoli. This procedure is with suitable technique neither very painful nor dangerous, and no ill-effects were observed to follow it : on the contrary in some cases it appeared to hasten resolution (as noted by Abrahams[1] during the 1918 influenza, and Stewart[28]).

In a few cases blood cultures were also made successfully, but in young children the technique of blood culture is often very difficult and in many cases I was unable to secure trustworthy results. Although many faucial swabs were also examined, it was found that no reliance could be placed on the evidence so obtained for the diagnosis of the organisms primarily responsible for the pneumonia.

With regard to the B. influenzæ it should be stated that no attempt was made to distinguish various strains, although para-influenzal bacilli and the bacillus of Bordet could be excluded. There is no doubt that several different strains showing definite morphological differences were encountered. The medium used for the cultivation of the B. influenzæ was agar with 10 per cent. citrated horse-blood heated to 83° C. after storage at room temperature for two or three weeks. The growth obtained was usually luxuriant.

Discussion of results.

Bacteriological results.—The 75 cases investigated here were selected from about 150 cases of pneumonia which occurred at the Grove Hospital in the measles epidemics during 1927–28 and 1929 to March, 1930. 52 belong to the former epidemic and 23 to the latter.

In all but one (Case 52), an attempt was made to determine the organism primarily responsible for the pneumonia, the additional case being one of death from scarlatinal nephritis five months after measles pneumonia.

B. INFLUENZÆ.—Organisms of the influenza group were demonstrated in 34 out of 74 cases (46 per cent.). Of these 34 cases, 22 occurred in the 51 cases from the 1927–28 outbreak, and 12 from the 23 cases of the 1929–30 epidemic.

In 23 cases out of 74 (31 per cent.) B. influenzæ was obtained from the lungs in pure culture.

In 5 instances B. influenzæ was associated with a hæmolytic streptococcus. These cases were all fatal, the combination apparently producing a very severe form of toxæmia with early heart failure.

PNEUMOCOCCI.—In 6 cases the pneumococcus was noted in addition to B. influenzæ, and in 21 cases (28·4 per cent.) pneumococci only, or pneumococci with non-hæmolytic streptococci were found.

In this connection it may be observed that Malloch noticed an association with B. influenzæ in the majority of cases of broncho-pneumonia from which he isolated the pneumococcus. Lyon found pneumococci more frequently than B. influenzæ in primary broncho-pneumonias, but recognized that the influenza bacillus was soon overgrown in these conditions.

It seems likely that in a number of the cases here returned as primarily pneumococcal the influenza bacillus might have been obtained had cultures been made at an earlier stage of the disease.

STREPTOCOCCI.—Streptococci were found alone in 9 cases (12 per cent.). In 6 cases hæmolytic streptococci were found, and in 3 cases streptococcus viridans only.

OTHER ORGANISMS.—Staphylococci and M. catarrhalis only were found in 7 cases, but the clinical course of the disease suggested strongly in more than one of these cases, that B. influenzæ might have been present at an earlier stage, or that it failed to grow in cultures from the lung.

Although these findings are sufficient to indicate the importance of the B. influenzæ in measles pneumonia, they probably under-estimate the frequency with which this group was present in these cases, on account of the indubitable tendency for these organisms to die out or be replaced by others as the disease progresses. The most acute forms of pneumonia encountered were associated with B. influenzæ, and examination of the lungs revealed fulminating interstitial inflammation with hæmorrhage (Fig. 1–4).

Clinical features.—In the more acute cases it is not difficult to distinguish the 'influenzal' type of pneumonia by clinical observation alone. The toxæmia and cyanosis are out of all proportion to the physical signs in the chest. The leucocyte count is very variable: a count below 10,000 is of serious

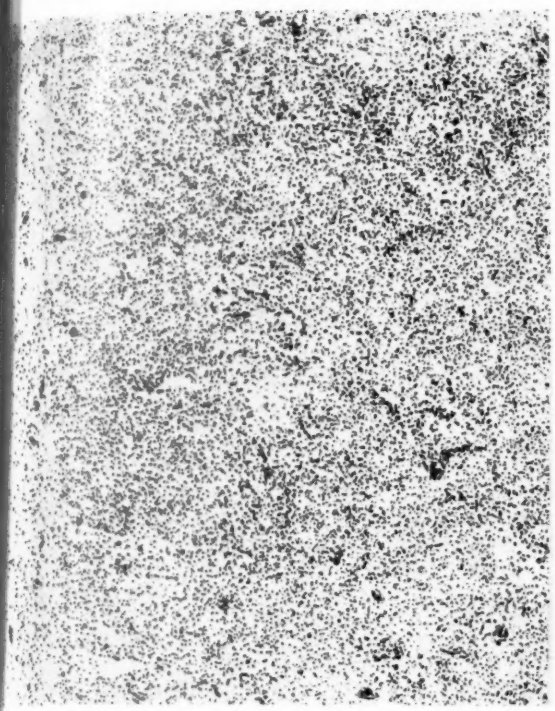

FIG. 1 ($\frac{1}{3}$-in. objective).
Section of lung of male aged 1 year 7 months, showing interstitial pneumonia of 28 days duration. The pleura is much thickened. There is no evidence of resolution. B. influenzæ were obtained in pure culture.

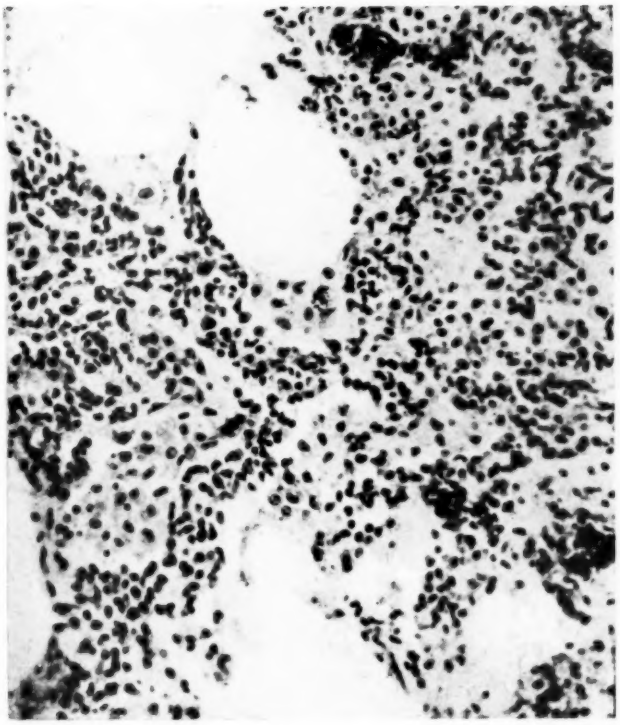

FIG. 2 ($\frac{1}{6}$-in. objective).
The same case as Fig. 1. Section shows proliferation of endothelial cells into the alveolar spaces. Macrophages can be seen removing blood pigment, the result of hæmorrhage at an earlier stage.

FIG. 3 ($\frac{1}{6}$-in. objective).
Section of lung of male aged 1 year, showing acute interstitial pneumonia of 13 days duration due to B. influenzæ. Proliferation of fibroblasts and endothelial cells has produced so much thickening of the alveolar walls, that the alveolar space is almost obliterated.

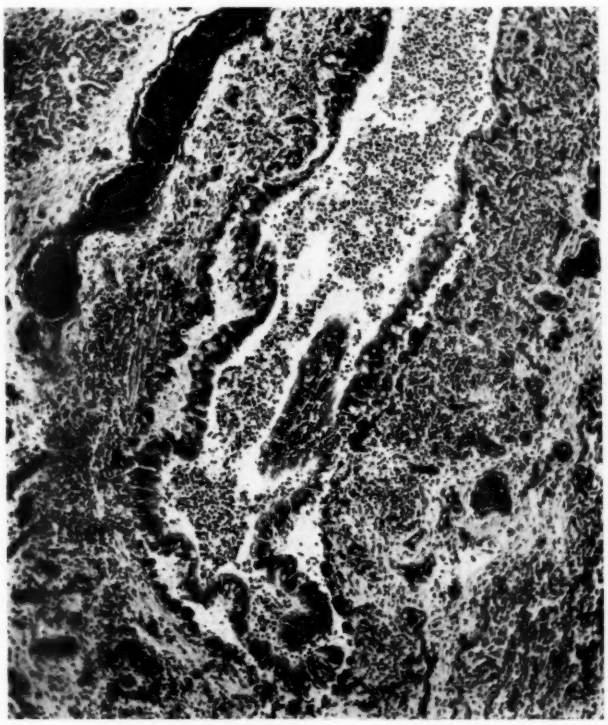

FIG. 4 ($\frac{1}{6}$ in. objective).
The same case as Fig. 3. Section through a bronchus showing desquamation of bronchial epithelium and engorgement of the peri-bronchial capillaries. The inflammation is, however, not so severe as in many cases since the basement membrane appears to be intact.

import, but unfortunately an apparently satisfactory leucocytic response is by no means an indication that the disease will pursue a favourable course (Table 3).

TABLE 3.

LEUCOCYTE COUNTS IN MEASLES PNEUMONIA.

B. influenzæ in pure culture			B. influenzæ with other organisms			Pneumococcus alone or with streptococci			Streptococci hæmolytic or viridans, predominating		
Case No.	Leucocytes	Result	Case No.	Leucocytes	Result	Case No.	Leucocytes	Result	Case No.	Leucocytes	Result
5	12,000	F	25	12,000	F	12	5,000	F	35	20,000	F
6	5,000	F	37	7,000	F	13	40,000	R	41	35,000	F
8	8,000	F	40	10,000	R	14	8,000	R	50	50,000	R
38	8,000	F	43	15,000	R	15	5,000	R	4	10,000	F
42	5,000	F	9	25,000	F	19	43,000	R	11	8,000	F
44	9,000	R	26	15,000	F	33	9,000	R	10	7,000	F
47	10,000	R	27	20,000	F	54	24,000	F	21	25,000	R
48	25,000	R	46	26,000	F	55	14,000	F	45	30,000	F
58	14,000	F	57	11,000	F	56	16,000	R	68	18,000	F
59	13,000	F							71	18,000	F
63	*35,000	R							72	20,000	F
66	13,000	F									
67	†40,000	R									
74	†45,000	R									
Average = 11,000 (uncomplicated cases)			Average = 15,600			Average = 18,200 (not significant owing to very high standard deviation of series)			Average = 22,000		
Average of 16 recoveries = 24,000.						Average of 27 fatal cases = 15,600.					

*Complicated by ac. strep. laryngitis. †Complicated by mild pertussis.

The heliotrope cyanosis which is a prominent feature of these cases appears of a nature similar to that which has been so often observed in true influenza. It is not abolished by inhalation of oxygen, and Haldane[8] has suggested that cyanosis of this kind may be due to alteration in the chemical constitution of the blood by a nitrite-producing organism (B. influenzæ possesses this power), the stable nitroso-hæmoglobin being produced in a manner analogous to that of the production of carboxy-hæmoglobin in carbon monoxide poisoning. In order to decide this point, it would of course be necessary to determine the dissociation curve of the blood in these cases: but there are reasons against accepting this hypothesis as an explanation of the cyanosis observed in the 'influenzal' pneumonias of measles.*

The degree of cyanosis is very variable: it may disappear with great rapidity and reappear as suddenly. This suggests a vasomotor mechanism, with a general weakening of the capillary tone. The state of the whole

*NOTE.—Abrahams[1] found that there was no loss in oxygen-carrying capacity of the blood in a series of cases of influenzal pneumonia examined by Haldane's ferricyanide method.

peripheral circulation resembles that observed in chilblains, and it seems likely that the calcium metabolism is seriously deranged.

The whole picture is strikingly different from the ordinary cyanosis of anoxæmia, when a large area of lung is consolidated and the respirations are shallow, as in ordinary lobar pneumonia. The physical signs are often equivocal: dullness at one base with distant breath sounds may suggest the presence of fluid in nearly half the cases examined, whereas it will only be discovered in about one case in fifty (Table 1). Some consonating rales at the bases may be the only signs during life in a case which shows extensive interstitial proliferation post mortem. The pneumococcal and streptococcal cases present the signs and follow the course of the classical broncho-pneumonia of children, though in some instances the streptococcal cases appear to resemble closely the B. influenzæ pneumonias, and this resemblance is especially close when a mixture of organisms is found in the lungs. The leucocyte counts tend on an average to be higher in the catarrhal pneumonias.

It is generally possible to diagnose a pure B. influenzæ pneumonia on clinical grounds alone.

Morbid Anatomy.—Difficulty in securing post-mortem examinations has limited the amount of evidence available, but an examination of the lungs in 8 fatal cases in which B. influenzæ was predominant revealed the changes characteristic of interstitial pneumonia.

In 3 of these cases (No. 6, 37, and 42) the condition was extremely acute. In one case (No. 59) it was of longer duration (28 days) and revealed the early stages of organization with fibrosis.

Three cases were examined in which hæmolytic streptococci were predominant, and these revealed severe catarrhal changes with purulent bronchiolitis, and early abscess formation (Fig. 5). In one (Case 17) there was a definite abscess of the lung which was adherent to the parietal pleura.

In one case (No. 46), B. influenzæ had been replaced by a hæmolytic streptococcus with the subsequent development of empyema, but no autopsy could be obtained.

In three cases in which the pneumococcus appeared to be the primary agent, the classical broncho-pneumonic lobular consolidation was found, together with catarrhal exudate into neighbouring alveoli. The same condition was found in one case in which only staphylococcus aureus and M. catarrhalis were discovered.

Sequelæ.—Very few sequelæ were noted in those cases which recovered, probably because they could not be observed over long enough periods. It is unfortunate that there is no means of following up cases discharged from L.C.C. institutions, since there is little doubt that many cases of chronic pulmonary disease which later find their way into the out-patient departments of general hospitals, can be traced back to an alleged attack of measles, often many years earlier (Leys[16]).*

*An examination of the history of 53 cases of non-tuberculous pulmonary fibrosis in children under 15 years of age made at Brompton Hospital in 1928 by Kitcat and Sellors[12] showed that the condition was to be attributed to measles alone in 14 cases (26 per cent.), to whooping cough alone in 8 (15 per cent.), and to a combination of both diseases in 16 (30 per cent.).

Bronchiectasis.—One case (No. 50) admitted with lobar pneumonia developed pertussis while convalescent, and in the space of a few weeks presented all the signs of acute bronchiectasis with a cavity at the right base.

I have observed acute bronchiectasis in three other cases (not included in this series) in children under three years of age who developed measles during the course of pertussis. As McNeil, Macgregor, and Alexander have pointed out this event is really the result of complete destruction of the walls of the smaller bronchi; every vestige of the original wall, including cartilage, disappears, and the bronchus is represented by a space bounded directly by

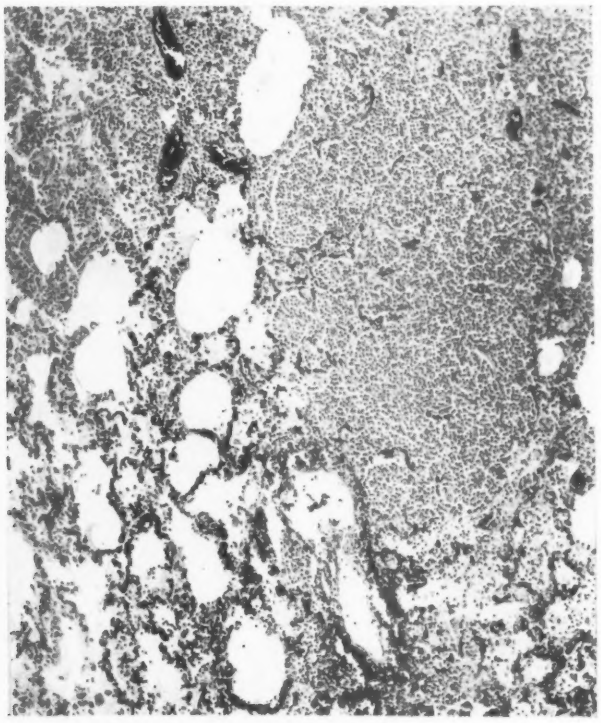

Fig. 5 ($\frac{1}{6}$-in. objective).

Male, aged 4 years. Broncho-pneumonia of 8 days duration due to strepto-coccus hæmolyticus. Section shows purulent bronchitis, with peri-bronchial consolidation and early abscess formation. Surrounding the abscess there is a zone of endothelial proliferation extending into the neighbouring alveoli.

consolidated alveoli. This state of affairs is more likely to be the end result of chronic infective processes, but the combination of measles and pertussis can bring it about in a surprisingly short space of time.

In one case (No. 52), the patient was considered on clinical grounds to be suffering from fibrosis of the lung subsequent to measles pneumonia five months earlier. This patient died from acute scarlatinal nephritis and a post-mortem examination of the lungs was made without revealing any notable fibrotic change.

Prognosis.—(1) THE AGE FACTOR.—In the 1927–28 epidemic 1,341 cases of pneumonia in measles occurred in M.A.B. (now L.C.C.) institutions with 541 deaths, these constituting 86 per cent. of the total deaths from measles during the epidemic. The case mortality, 40 per cent., is only an approximation to the truth because, in any large series, there may be a reasonable doubt in mild cases, whether broncho-pneumonia or simple bronchitis should be diagnosed, and various criteria are used in compiling statistical tables in different institutions. During this period 100 cases of pneumonia occurred at the Grove Hospital with 47 deaths. I should regard 45 per cent. with a probable error of 2.5 as a reasonable figure for the pneumonia case mortality in this epidemic.

In the present series the case mortality is not significant owing to the pre-emptive selection of fatal cases.

With regard to the prognosis in any given case, the factor of age is so well known that little remains to be said on this score, though it is perhaps worth while to mention that the low mortality among adults only holds for communities in which measles is widespread throughout the child population.

The serious outbreaks in army camps, recorded more particularly in America, are evidence of this. During the American Civil War, there occurred 67,763 cases of measles in the armies with 4,246 deaths, a case mortality of 6.27 per cent., which is closely similar to that of an ordinary epidemic among London children. In 1864 at Benton barracks, Surgeon Ira Russell had 675 cases of measles with 130 deaths, that is to say, a case mortality of just over 20 per cent. The congregation of a large number of susceptibles of a similar type, (in this case of approximately the same age), appears to lead to a rise in the fatality rate. It is probable that any adult contracting measles in London is likely to be relatively insusceptible to the disease to have escaped it for so long, but this cannot apply to immigrants from regions in which measles is not prevalent; so that it is possible that the high resistance of such people to pneumonia may be due to the fact that they can withstand the secondary invading organisms which are lethal to children, but succumb to their own when they are herded together in any large numbers.

It is worth noting that inbeciles are unusually susceptible to measles, and the mortality is high among them, owing to their low resistance to broncho-pneumonia. This fact accounts for apparent irregularities in the fall of case mortality with increasing age seen in some statistical tables.

(2) PREVIOUS HISTORY.—A history of previous respiratory infection does not appear to be of much prognostic importance. In the present series, 52 cases had no history of any previous illness, and of these 36 died; 22 cases had a history of previous pneumonia or bronchitis, and 13 of these were fatal.

Eight cases gave a history of recent pertussis and 5 of these were fatal. There seems little doubt that measles is especially dangerous in a child which has recently suffered from pertussis. Very recent scarlet fever undoubtedly increases the risk of streptococcal empyema, and I have observed this sequence of events in three cases at the Grove Hospital.

The importance of rickets, though well known, is not easy to assess with any degree of accuracy, but the fact that the mortality from measles falls so

heavily on those classes among whom rickets is prevalent is an indication of its significance.

From the standpoint of bacteriology the most benign cases appear to be those in which the pneumococcus alone is present. Hæmolytic streptococci, alone or associated with B. influenzæ, are far more dangerous. A pure influenzal infection probably occupies an intermediate position regarding fatality (Table 4).

TABLE 4.

BACTERIOLOGICAL ANALYSIS OF 74 CASES OF MEASLES PNEUMONIA WITH DEATH RATE.

Bacteriological group	Epidemic	Total cases	Death rate		Empyema
			Total	per cent.	
I B. influenzæ alone.	1927—28	13	10	76	
	1929—30	10	7	70	
	Total ...	23	17	73·9	
IIA B. influenzæ with pneumococcus.	1927—28	4	1	25	
	1929—30	1	1	100	
	Total ...	5	2	40	
IIB B. influenzæ with streptococci or other micro-organisms.	1927—28	5	5	100	1
	1929—30	1	1	100	
	Total ...	6	6	100	1
III Pneumococci alone or with streptococci.	1927—28	17	6	35·3	
	1929—30	4	3	75	
	Total ...	21	9	42·9	
IV Streptococci alone.	1927—28	4	3	75	
	1929—30	6	6	100	
	Total ...	10	9	90	
V Staphylococcus and other micro-organisms.	1927—28	7	5	71·4	
	1929—30	0	0		
	Total ...	7	5	71·4	
VI Unclassified.	1927—28	2	2	100	
	1929—30	1	1	100	
	Total ...	3	3	100	

The leucocyte count appears to have little prognostic importance in any given case, but a very low count with B. influenzæ present is of serious import (Table 3).

Summary and conclusions.

(1) Micro-organisms of the influenza group were demonstrated in the lungs in 46 per cent. of a series of cases of pneumonia complicating measles occurring during successive epidemics in London. It is probable that this is an underestimate of the frequency of these organisms in measles pneumonia.

(2) Evidence is brought forward in support of the hypothesis that acute interstitial pneumonia is a frequent and important complication of measles, and that this condition is to be attributed to the agency of B. influenzæ.

(3) Acute interstitial pneumonia can be distinguished clinically and pathologically from other forms of pneumonia, and may be regarded as an important cause of non-tuberculous chronic pulmonary disease in later life.

(4) The conclusion is reached that cases of lobar and broncho-pneumonia can be safely nursed in general measles wards without risk of dissemination, if reasonable precautions are taken against overcrowding.

(5) Hæmolytic streptococci are less important as a cause of broncho-pneumonia in children than in adults with measles. The comparative rarity of empyema as a complication of measles in children is held to support this view.

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OBSERVATIONS ON THE MILK OF NEW ZEALAND WOMEN

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PART I. THE DIURNAL VARIATION IN THE FAT CONTENT OF HUMAN MILK.

The composition of human milk has been the subject of many researches but reference to the literature indicates that little attention has been paid to the question of diurnal variation in the fat content of the milk. No definite approach to regularity in this variation has hitherto been observed.

Reiset[1] as far back as 1849 observed that the fat percentage of human milk was decreased and the amount of milk increased by extending the time between successive milkings. Helbich[2] from the examination of the milk of six wet nurses concluded that the fat percentage of human milk expressed at four-hourly intervals was highest at 10 a.m. and 2 p.m. Talbot[3] from the examination of the milk of six women concluded that the fat percentage of milk expressed at three-hourly intervals was highest at noon or later on in the day. The data submitted show, however, that two of his six cases did not support his conclusion. Myers[4] records the analysis of the milk of three women whose breasts were expressed at different times of the same day: variations in the composition were noticed and the paper is concluded with an apt quotation of John Thomson 'that the composition of human milk, like other secretions, varies from time to time and even during the course of the day.'

The object of the present investigation was to record, under rigidly controlled conditions, the limits in the diurnal variation in the fat percentage of the milk of a large number of women in order that any regularity of variation might become apparent. In such an enquiry meticulous attention must be paid to the collection of the samples which are to form the basis of the research, for, unless the samples are carefully taken under strictly comparable conditions, the deductions must be open to question however carefully analysis of the samples is carried out. Additional precautions are needed in investigating human milk because of the recognized influence of psychological factors.

For the collection and analysis of the samples employed in the research the following conditions were postulated:—

(a) The women must be healthy and well nourished, and must have a fairly abundant milk secretion.

(b) The milk in any one experiment must be expressed by the same operator at regular intervals.

(c) The greatest care must be taken to avoid loss of fore milk by leakage, and that the after milk or "strippings" should be expressed as completely as possible.

(d) The mother should be kept in a contented state of mind, by cheerful talk and sympathy, during the whole process of expression.

All samples of milk were expressed either by the writer or, as in Series 4, under the personal supervision of the writer. The precautions taken in procuring the samples are dealt with in the experimental part of the paper.

Four separate series of experiments were carried out during the past eighteen months and the diurnal variations in the fat content of the milk of thirty women were recorded. This has involved the determination of the fat percentage of 332 samples.

Eighty-one samples were analysed completely for fat, protein, sugar and ash, in order to determine the question of diurnal variation in the constituents other than fat.

The diurnal variation in the fat content of the milk of four women was determined on seven different days, one week elapsing between each experiment. The results are expressed graphically in Graph III.

In 27 cases, the milk was expressed from one breast only throughout the day. In three cases, the milk of both breasts was expressed separately and the samples independently analysed.

The mothers from whom the samples were taken were healthy, well nourished women of European stock. With two exceptions, all were born in New Zealand. Their ages ranged from 17 to 38 years, but 5 only were above the age of 28 years. The mothers included in the first three series were temporary residents of the Karitane Home, Dunedin. Those included in the fourth series were, with one exception, residents of St. Mary's Home (for unmarried mothers), Otahuhu, Auckland, N.Z.

The infants were, with the exception of one case of pyloric stenosis, healthy and thriving on their mothers' milk. Their ages ranged from 5 to 36 weeks. Four of the babies received a small complement of modified cow's milk; the remainder were adequately suckled by their mothers.

It is commonly stated that fore milk has a much lower fat percentage than end milk or strippings. Analyses made during this investigation bear out this contention. Care was therefore always taken to empty the breasts as completely as possible. It is assumed that some milk remained in the deeper recesses of the mammæ at the end of expression, for Gaines[5] who conducted a series of careful experiments on goats proved that hand milking did not empty the goat's udder as efficiently as did the suction of the kid, but he concluded that hand milking ensured a uniform degree of emptying at each milking. Similarly, the writer contends that when hand expression is done by one experienced individual an uniform degree of emptying will take place at each expression.

Great attention was paid to the psychological factor for it is generally recognized amongst farmers that even in cattle the holding back of the milk

will take place if the animal is not completely at its ease. The same psychological factor is by no means uncommon amongst nervous and excitable nursing mothers ; hence a practice was invariably made of securing the confidence and friendship of the mother before taking a sample of her milk.

It was found that the large flat muscular type of breast could not be emptied effectively by manual expression, and for this reason samples were not taken from women with this type of breast.

Method of investigation.—The milk was obtained from the breast by hand expression in the following manner. The breast was grasped at the proximal boundary of the areola by thumb and fore-finger of the operator's right hand ; the left hand was used to steady the breast. Each pressure of the fingers was accompanied by a downward and forward movement without any manipulation or squeezing of mammary tissue. The milk flowed freely from the breast in a series of jets.

During the course of an experiment, the infant of the mother in question was allowed one breast only throughout the 24-hour period of the experiment, and was weighed before and after going to that breast. When the infant had been fed from one breast, the entire content of the other was expressed, well mixed, and a sample taken for analysis. The remainder of the milk was given to the baby by bottle. In general, the quantity of milk obtained by expression was less than the amount obtained directly from the breast by the baby. This is in accordance with Gaines's results already mentioned. In each case the amount of milk obtained by the baby indicated the amount of milk that might be expected as the result of expression. In some instances, where the flow had apparently ceased and yet the amount of milk expressed was considerably less than had been obtained by the baby, a rest for a minute or two, together with gentle stroking of the breast, again produced a free flow of milk. Had not this after milking been carried out, the richest portion of the milk would have been missed and a grave error would have been introduced.

Women with an abundant milk secretion frequently stated that when the infant commenced to suck from one breast, at the 6 a.m. feeding in particular, the milk simultaneously leaked away from the other breast. This statement was confirmed by personal observation, and it is in accordance with the observations of Gaines on the mechanism of milk secretion in lactating animals. Care was therefore taken to collect all milk which leaked away from the one breast as a result of the general stimulus to milk flow provided by the sucking of the child at the other breast. Thus no fore milk was lost.

In order to give a mother confidence and at the same time assure her that the process of expression was simple and not painful, one breast was expressed as completely as possible at the feeding time before the actual experiment was commenced. Succeeding specimens were then obtained at four-hourly* intervals during the day, with an eight-hour interval during the night. Five specimens were thus obtained at the usual feeding times, 6 a.m., 10 a.m., 2 p.m., 6 p.m. and 10 p.m.

*In 3 cases, the specimens were obtained at three-hourly intervals throughout the day, commencing at 6 a.m.

Four separate series of observations were made. In the first three series, every sample of milk, with one exception, was expressed by the writer. In the fourth, the mothers, who were all skilled expressors, did their own expressing under the supervision of the writer. In this series the final expression took place at 11 p.m. after the mothers had had between two and three hours' sleep.

Analysis.—Four separate series of analyses were made.

I. In the first series the author determined, by the Babcock method, the percentage of fat in thirty samples of milk expressed by herself from six women at the four-hourly intervals. The mean curve for the diurnal variation of Series I, as shown in Graph I, was sufficiently striking to demand confirmation by other series of experiments in which the analyses were conducted by independent observers.

II. In the second series (comprising 7 individual cases) the diurnal variation in the fat and other constituents of the milk was determined. Complete analyses of 81 samples of human milk were made by the Dunedin Government analyst, Mr. L. S. James, M.Sc., F.I.C.

III. In the third series (8 cases) the fat only was determined. This also was done by Mr. L. S. James.

IV. In the fourth series (9 cases) the analyses were carried out by Mr. K. M. Griffen, M.Sc., F.I.C., Auckland Government analyst, and only fat determinations were made except in special cases where the effect of diet on milk production was being studied.

In the analyses conducted by the Government analysts the fat was determined by the Gerber process; the protein by the Kjeldahl method; the ash by incineration; and the sugar by difference.

Average fat.—Since the weight of milk obtained is not the same at each expression, the average percentage of fat on one day is not identical with the arithmetical mean of the five fat percentages recorded on that day. The average percentage of fat in the day's milk is obviously found by dividing the total weight of the fat by the total weight of the milk expressed and multiplying by 100. The averages in the annexed tables are calculated on this basis.

Results.

The results of the investigation are given in the following tables and graphs.

Table 1.—Series I—IV, showing the diurnal variation in the fat content of the milk of twenty-seven women expressed at four-hourly intervals.

Table 2.—Showing the diurnal variation in the fat content of the milk of three women expressed at three-hourly intervals.

Table 3.—Showing the diurnal variation in the constituents of the milk other than fat.

Graph I.—Showing the mean curves for the diurnal variation in the fat content of the milk of each series.

Graph II.—Showing the average curves of diurnal variation of all the series in respect to fat content and volume.

TABLE I.

SHOWING THE DIURNAL VARIATION IN THE FAT CONTENT OF THE MILK OF TWENTY-SEVEN WOMEN.

Series	Case No.	Age weeks	6 a.m.		10 a.m.		2 p.m.		6 p.m.		10 p.m.		Average
			Fat %	c.cm.	Fat %	c.cm.	Fat %	c.cm.	Fat %	c.cm.	Fat %	c.cm.	Fat %
I	1	30	2·8	142	5·2	83	4·1	98	3·7	53	3·7	75	3·7
	2	24	4·2	135	7·3	60	5	45	5·4	60	6·2	53	5·3
	3	23	2·8	120	4·5	68	7·7	98	5·5	75	5·8	53	5·1
	4	20	3·2	135	5·4	60	4·5	75	4·2	75	3·9	45	4
	5	11	3·2	128	5·3	60	4·8	60	5	60	4·9	45	4·3
	6	4	3·7	113	5·7	30	5·6	68	4·6	38	4·6	90	4·5
		Av'age	3·3	129	5·6	60	5·3	74	4·8	60	4·8	60	4·5
II	1a	24	4·1	135	7·7	83	5·9	60	4·4	53	4·2	60	5·2
	7	16	4·1	135	7·9	90	5·05	60	5·05	75	4·9	60	5·3
	8	34	3·9	165	5·7	83	4	60	5·2	53	4·7	90	4·6
	9	27	3·2	225	6·7	83	5·4	90	4·7	83	—	—	4·4
	10	16	(R)3·4	90	4·5	45	3·95	68	3·8	60	3·3	38	3·7
			3	127·5	4·1	78·5	3·3	90	3·5	90	3·3	75	3·3
			(L) 2·65	165	3·7	112	2·7	113	3·2	120	3·3	113	3·07
	c11	6	(R)3	83	4·6	38	3·7	30	3·8	63	4·1	38	3·6
			2·8	116.5	4·6	56·5	3·9	49	3·7	63	3·9	49	3·5
			(L) 2·65	150	4·5	75	4·1	68	3·6	75	3·7	60	3·5
	12	7	2·7	90	4	60	3·9	60	3·8	53	4·2	45	3·6
	13	18	(R)3·6	450	4·65	195	3·2	158	3·5	165	2·95	165	3·6
			3·5	457·5	4·7	201·5	3·3	158	3·5	165	2·8	165	3·5
			3·4	465	4·7	210	3·4	158	3·5	165	2·75	165	3·5
		Av'age	3·45	182	5·7	92	4·3	78	4·2	79	4·0	78	4·2
III	14	20	2·55	120	5·3	75	5·05	75	5·15	75	5·2	60	4·3
	15	36	5	143	9	60	5·4	64	4·6	75	5·7	90	5·6
	16	12	2·7	158	4·8	90	4	83	3·6	83	3·9	75	3·5
	18	3	3·2	60	4	30	3·8	34	3·4	30	3·3	26	3·48
	19	7½	3	120	5·2	53	4·2	53	3·8	53	3·5	45	3·7
	20	7	4·7	105	7·8	75	5·4	45	4·6	45	5·4	45	5·2
		Av'age	3·5	118	6	64	4·7	59	4·2	60	4·5	57	4·3
			6 a.m.		10 a.m.		2 p.m.		6 p.m.		11 p.m.		
IV	21	6	4·06	267	5·48	132	4·4	132	4·1	142	4·2	150	4·29
	22	15	2·86	180	4·71	111	3·91	99	3·48	93	3·24	108	3·51
	23	25	2·9	126	5·06	75	4·54	66	3·38	48	2·9	69	3·7
	24	15	3·0	129	5·2	60	4·1	72	4·1	69	3·5	75	3·8
	25	21	4·6	90	6·5	60	6·2	60	5·5	52	4·9	60	5·5
	26	5	3·8	127	4·1	82	2·9	78	3·6	75	3·3	82	3·57
	27	8	3·6	127	4·5	78	4·8	60	4·55	82	4·45	67	4·28
	30	36	2·45	138	5·3	78	4·8	69	3·5	84	3·4	87	3·6
		Av'age	3·4	147	5·1	84·5	8·5	79·5	4·1	80·5	3·7	87	4·0

TABLE 2.

SHOWING THE DIURNAL VARIATION IN THE FAT CONTENT OF THE MILK OF THREE WOMEN EXPRESSED AT THREE-HOURLY INTERVALS.

Case No.	Age	6 a.m.		9 a.m.		12 noon		3 p.m.		6 p.m.		9 p.m.	
		Fat %	c.cm.	Fat %	c.cm.	Fat %	c.cm.	Fat %	c.cm.	Fat %	c.cm.	Fat %	c.cm.
17	3½	3·2	165	5·8	82	4·2	67	4·3	82	4·2	60	4·1	60
28*	6	2·9	105	4·1	52	3·4	45	4·0	56	2·7	45	3·4	75
29*	4	3·6	156	4·9	84	3·8	72	3·3	63	3·3	57	3·4	66
	Average	3·2	142	4·9	72·6	3·8	61·3	3·9	67	3·4	54	3·6	67

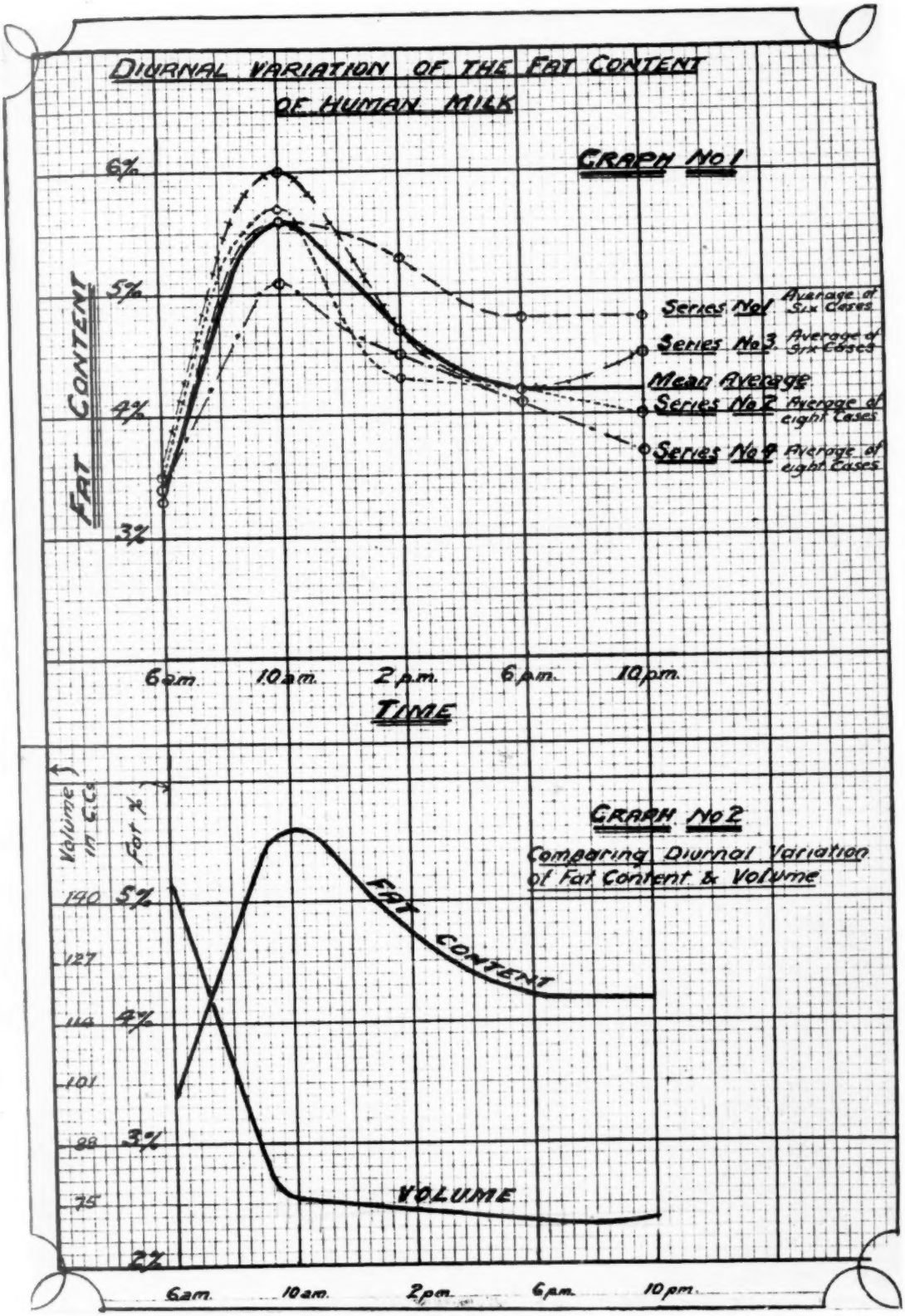
* In Cases 28 and 29 the last expression took place at 11 p.m. This probably accounts for the comparatively large volume expressed after a five-hour interval of rest.

TABLE 3.

SHOWING THE DIURNAL VARIATION IN THE CONSTITUENTS OTHER THAN FAT OF THE MILK OF SEVEN WOMEN.

Case No.		6 a.m.				10 a.m.				2 p.m.				6 p.m.				10 p.m.			
		Protein	Sugar	Ash	T.Sds.	Protein	Sugar	Ash	T.Sds.	Protein	Sugar	Ash	T.Sds.	Protein	Sugar	Ash	T.Sds.	Protein	Sugar	Ash	T.Sds.
1a		1·06	7·37	·18	12·71	1·17	7·3	·19	16·36	1·05	7·17	·19	14·31	1·12	7·3	·19	12·96	1·09	7·37	·19	12·85
7		1·21	7·17	·19	12·72	1·26	7·09	·21	16·46	1·23	7·26	·2	13·74	1·14	7·12	·19	13·5	1·13	7·12	·2	13·35
8		1·06	6·57	·17	11·7	1·06	6·89	·18	13·83	1·10	7·13	·17	12·4	1·12	7·38	·2	13·9	1·07	7·36	·2	13·33
9*		1·09	7·36	·19	11·79	1·15	7·04	·18	15·07	1·11	7·15	·19	13·8	1·11	7·31	·19	13·3	—	—	—	—
10	R	1·59	6·85	·25	12·09	1·59	6·9	·25	13·24	1·62	7·33	·24	13·14	1·64	7·09	·27	12·8	1·63	7·17	·26	12·61
	L	1·23	6·49	·21	11·58	1·23	7·33	·21	12·47	1·21	7·57	·21	11·09	1·19	7·42	·22	12·03	1·27	7·32	·22	12·11
11		1·25	7·47	·2	11·57	1·39	7·11	·21	13·21	1·35	7·23	·21	12·89	1·34	7·39	·2	12·58	1·25	7·22	·2	12·37
13		1·15	7·39	·18	12·32	1·14	7·25	·18	13·22	1·10	7·29	·18	11·77	1·02	7·41	·19	12·12	1·09	7·31	·19	11·54
		1·13	7·54	·19	12·26	1·15	7·26	·19	13·3	1·11	7·41	·19	12·11	1·08	7·35	·19	12·12	1·09	7·43	·18	11·14

* Child fed 4 times in 24 hours.


DIURNAL VARIATION OF THE FAT CONTENT OF HUMAN MILK
GRAPH No 1
6%
5%
4%
3%
FAT CONTENT
Series No1 Average of Six Cases
Series No3 Average of Six Cases
Mean Average
Series No2 Average of eight Cases
Series No4 Average of eight Cases
6 a.m.
10 a.m.
2 p.m.
6 p.m.
10 p.m.
TIME
GRAPH No 2
Comparing Diurnal Variation of Fat Content & Volume
Volume in C.Cs
Fat %
190
127
114
101
88
75
5%
4%
3%
2%
FAT CONTENT
VOLUME
6 am.
10 am.
2 pm.
6 pm.
10 pm.

GRAPHS I & II.

Discussion of results.

The average fat percentage for the day was between 3 and 4 in 16 cases (53·3 per cent.); between 4 and 5 in 8 cases (26·7 per cent.); and above 5 in 6 cases (20 per cent.).

The mean average fat percentage was 4·18. This figure is higher than that given by Richmond[6] but is lower than that given by various continental writers. It must be noted, however, that 53·3 per cent. of the cases investigated showed an average fat percentage between 3 and 4.

The highest average fat percentage for the day was 5·4, and the lowest 3·2. The highest fat percentage of a single sample was 9, and the lowest 2·1.

The milks with the high average fat content showed the greatest diurnal variation; one case showed a difference of 4·9 per cent. between the highest and lowest values for the day.

Four of the six children receiving milk containing over 5 per cent. of fat were afflicted with infantile eczema; they were, however, all thriving well on their mothers' milk, one case (Case 15) being 4 lb. above the average weight of a child the same age (9 months).

The highest protein in a single sample was 1·64 per cent. and the lowest ·8 per cent.* The child, who was receiving the milk with the low protein content (·8 per cent.) was 4 lb. below the average weight of a child of the same age (9¼ months).

The average protein percentage of the milk of the cases investigated was 1·2. This figure agrees with that given by Richmond.

The highest ash in a single sample was ·27 per cent. and the lowest ·17 per cent.

In every case the largest volume of milk obtained at a single expression was recorded at 6 a.m. The average volume obtained at the specified times are recorded in Graph II. The largest volume expressed from a subject during the twenty-four hour period was 2,355 c.cm. This amount was obtained from the two breasts of a mother of twins.

In Series I the highest fat percentage for the day was found at 10 a.m. in five of the six cases investigated. The lowest fat percentage for the day was found at 6 a.m. in all of the six cases.

In Series II the highest fat percentage for the day was found at 10 a.m. in seven of the eight cases investigated. The lowest fat percentage for the day was found at 6 a.m. in seven of the eight cases.

In Series III the highest fat percentage for the day was found at 10 a.m. in all of the cases investigated. The lowest fat percentage for the day was found at 6 a.m. in five of the six cases.

In Series IV the highest fat percentage for the day was found at 10 a.m. in seven of the eight cases investigated. The lowest fat percentage for the day was found at 6 a.m. in seven of the eight cases.

Thus in 24 of the 27 cases investigated (i.e., 89 per cent.) the highest fat percentage for the day was found at 10 a.m. and in twenty-four of the cases investigated the lowest fat percentage for the day was found at 6 a.m.

*The mother, who produced the milk of such low protein content, was a strict vegetarian who absolutely excluded animal protein from her diet. Her protein ration was obtained almost entirely from whole-meal bread and peanuts—of the latter she consumed 6·2 oz. daily.

The average diurnal variation for each series and the average variation for all cases is represented graphically in Graph I.

In the three cases investigated, where the milk was expressed at three-hourly intervals throughout the day commencing at 6 a.m., the fat percentage was found to be highest at 9 a.m. in all three cases.

No diurnal variation in the constituents of the milk other than fat was observed.

The foregoing results and the graphs traced from them indicate the existence of a definite diurnal variation in the fat content of human milk. In the opinion of the writer, the results warrant the enunciation of the following law :—

> If all precautions are taken to secure the fore milk, middle milk and end milk present in the human breast, and if expression takes place at regular four-hourly intervals from 6 a.m. until 10 p.m., the fat percentage is in general lowest at 6 a.m., highest at 10 a.m., high at 2 p.m. and decreases as the day advances.

When it is borne in mind that physiological functions tend to show irregularities due to psychological, digestive, and other disturbances, as well as those characteristic of the individual subject, it is surprising that as much evidence of the existence of a general law has been observed. It is, however, obvious that the general rule or law of diurnal variation of fat content of human milk should not be accepted as a general application until it has been carefully tested by other observers working on a much larger number of rigidly controlled cases. It is also clear, when it is seen how great the diurnal variation in the fat content of human milk can be, that deductions based on the analyses of milk expressed at one time of the day only must be liable to very grave error.*

Summary of Part I.

(1) The diurnal variation in the fat content of the milk of thirty New Zealand women has been investigated.

(2) The results indicate that it usually takes place according to the following law :—

> If all precautions are taken to secure the fore milk, middle milk and end milk present in the human breast, and if expression takes place at regular four-hourly intervals from 6 a.m. until 10 p.m., the fat percentage is in general lowest at 6 a.m., highest at 10 a.m., high at 2 p.m. and decreases as the day advances.

(3) No diurnal variation in the constituents of human milk other than fat was observed.

(4) The mean average composition of the milk of the women investigated was :—fat 4·18 per cent., protein 1·2 per cent., ash ·22 per cent., and sugar 7·21 per cent. In 53·3 per cent. of the cases, the fat percentage was between 3 and 4, the average of these cases being 3·57.

(5) The importance of a knowledge of the law of diurnal variation is emphasized.

*Probably the high figure given by Wardlan and Dart[7] for the average fat percentage of the milk of Australian women is due in part to the fact that all samples of milk were expressed at 10 a.m.

PART II. THE EFFECT OF DIET ON THE SECRETION OF HUMAN MILK.

The object of the present investigation was to determine the effect of diet on the secretion of human milk.

The effect of diet upon the milk production of the cow is a problem which is constantly engaging the attention of dairy scientists. The results obtained by many workers in this field are contradictory, but with reference to certain findings a general opinion is entertained. Meigs[8] gives a comprehensive review of the subject and concludes that protein stimulates milk secretion and thus increases milk yield, and that the composition of milk may be affected by the feeding of certain diets.

With reference to the effect of diet on human milk production, the text-books in general state that provided the diet of a nursing mother is adequate, changes in any one of the food constituents of the diet will not appreciably affect the quality or quantity of her milk. Reference to the original literature shows that all too little work has been done on this important subject.

Engel[9] maintained that provided there was an adequate amount of fat in the diet of the nursing mother, an increase in the fat content of the diet did not increase the fat percentage of her milk. Czerny and Keller[10] conclude that the milk of nursing mothers cannot be permanently influenced by the food except in those instances when they are partially starved. Hoobler[11] investigated the effect of diet on the quality and quantity of the milk of two women. He concluded that a diet of a caloric value between 2,400—2,900 calories with a protein ratio of 1 : 4 was optimum diet for a nursing mother. He also concluded that animal protein in the diet was superior to vegetable protein. Bell[12] added small quantities of rice, tapioca or cream to a usual hospital diet and fed some mothers on one diet and others on another. She concluded from her experiments that the different diets given had little effect upon the composition of the milk.

The present work was carried out at St. Mary's Home, Auckland, N.Z. The mothers were taken into the home on the understanding that they were to reside there for six months after the birth of their infants and they were encouraged in every way to breast feed during the entire period. The Institution food was plain, wholesome and plentiful. The mothers appeared to have excessive appetites, a fact which is not surprising as they did all the manual labour of the home, such as milking cows, washing clothes, scrubbing floors and gardening.

As a routine practice, the mothers were taught the technique of hand expression during the puerperium. They became so proficient in the art that it was considered advisable in this investigation to allow them to express their own milk under supervision. Before selecting the special cases for the diet experiments, all the mothers in the home were carefully observed over a period of a fortnight. The diurnal variation in the fat content of the milk of each was estimated in the same way as detailed previously. These cases constitute Series IV in Part I of this paper.

As a result of these observations, it was possible to select suitable cases for the present investigation and five of the most trustworthy, keen and intelligent mothers were selected. Four of these were completely feeding their babies ; one with a slightly inadequate milk supply was chosen with the object of increasing her supply.

The mothers were healthy and active. Their ages ranged from 17 to 27 years. The infants were healthy and thriving, their ages ranging from 4 to 18 weeks.

Methods of investigation.—The five mothers selected were subjected to seven consecutive weeks of dieting under strict supervision. The diets were given in the following sequence: (1) Institution (St. Mary's Home Diet), (2) High Protein, (3) Institution, (4) High Protein + Vitamin B*, (5) High Sugar, (6) High Fat, (7) Low Protein. Each mother was fed for a period of 7 days on a specific diet. The food consumed by her was weighed and then calculated in terms calories, protein, fat and carbohydrate. It was not possible to revert to the Institution diet after each special period of dieting without unduly prolonging the duration of the whole experiment.

For 6 days, the babies were fed from both breasts at four-hourly intervals during the day and at eight-hourly intervals during the night, and test-weighed. Any milk remaining in the breast after feeding was expressed and measured.

On the 7th day, after 6 days' observation on a specific diet, the baby was fed from one breast only throughout the twenty-four hour experimental period and test-weighed, and the other breast was emptied as completely as possible by hand expression and the volume of milk measured. Thus the total yield of milk in the twenty-four hours was obtained.

The fat percentage of each expression was estimated in order to observe the effect of diet on the diurnal variation in the fat content of the milk. The results are tabulated in Table 6 and expressed graphically in Graph III.

The sample of milk which was analysed for protein, ash, sugar and total solids was a mixture of samples taken from each of the five daily expressions.

The analyses were conducted by the Auckland Government analyst, Mr. K. M. Griffen, M.Sc., F.I.C. The protein was determined by the Kjeldahl method; the fat by the Gerber process; the ash by incineration; the sugar by difference. The actual average fat percentage of the daily yield was computed in the same way as detailed in Part I of this paper.

Diets.—The caloric value of the Institution diet consumed by the mothers in question was in the vicinity of 3,000 calories. An attempt was therefore made to keep the caloric value of the test diets in the neighbourhood of 3,000 calories. This figure was unavoidably exceeded in Diets V and VI.

The protein content of the Institution diet was approximately 90 grm., therefore the protein of the test diets (other than the high and low protein diets) was kept approximately at the original amount.

According to the particular diet used, large increases in the protein, carbohydrate or fat constituents were employed.

The details of the diets of the mothers are tabulated in Table 4.

The mothers had vigorous appetites and found no difficulty in consuming the food set before them.

The effects of different diets on the milk secretion of the five mothers are tabulated in Tables 5 and 6.

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*B. Sure[13] experimenting with rats proved conclusively that the vitamin-B requirement of the lactating rat was considerably greater than for its mere growth. Vitamin-B (in the form of marmite) was therefore given to the nursing mother to ascertain whether its addition to the diet had any beneficial effect on human milk secretion.

TABLE 4.

GIVING THE DETAILS OF THE DAILY DIETS OF EACH OF THE FIVE MOTHERS.

Name	Diet	Calories	P : C+F	Carbo-hydrate	Fat	Protein	Remarks
				grm.	grm.	grm.	
Margaret	Institution	3,168	1 : 7·8	469	95	88	Plain, wholesome diet. Large quantities of bread and porridge. Puddings.
Daphne		3,198	1 : 7·7	470	97	90	
Flossie		3,082	1 : 7·9	450	96	84	
Mona		3,012	1 : 7·8	433	96	84	
Nancy		3,201	1 : 7·6	468	98	91	
Margaret	High protein	3,069	1 : 4	410	84	148	This diet included 3 eggs, 1,200 c.cm. skimmed milk, 180 grm. fish, 120 grm. meat.
Daphne		3,085	1 : 4	403	88	150	
Flossie		3,932	1 : 4	372	87	143	
Mona		2,804	1 : 3·9	347	87	140	
Nancy		3,152	1 : 4	408	92	152	
Margaret	High protein + vitamin B	2,944	1 : 3·99	379	86	144	As above plus 3 grm. marmite.
Daphne		2,985	1 : 3·9	385	86	148	
Flossie		2,886	1 : 3·99	374	84	141	
Mona		2,728	1 : 3·8	337	84	138	
Nancy		2,952	1 : 3·9	377	86	148	
Margaret	High sugar	3,836	1 : 9·4	630	95	90	This diet included 90 grm. dates, 30 grm. raisins, 60 grm. jam, 150 grm. iced cake, 60 grm. marshmallow sweet pudding.
*Daphne		3,978	1 : 9·5	654	99	92	
Flossie		3,935	1 : 9·7	646	99	89	
Mona		3,798	1 : 9·7	618	98	86	
Nancy		4,001	1 : 9·4	656	100	93	
Margaret	High fat	4,430	1 : 10·9	411	255	91	This diet included 150 c.cm. cream, 45 grm. bacon, 30 grm. fat ham, 30 grm. butter, 40 grm. dripping, 60 grm. shortbread, suet pudding or pastry.
Daphne		4,386	1 : 11	407	253	89	
Flossie		3,995	1 : 11	375	229	80	
Mona		4,303	1 : 11·4	382	265	86	
Nancy		4,461	1 : 10·8	420	254	92	
Margaret	Low protein	2,848	1 : 10·2	354	123	62	This diet included much green salads, pastry and vegetable soup — inevitably a comparatively high fat diet.
Daphne		2,861	1 : 10·2	357	123	62	
Flossie		2,779	1 : 10·4	340	123	59	
Mona		2,783	1 : 10·3	340	123	60	
Nancy		2,862	1 : 10·2	357	123	62	

* Average of 4 days diet : had bilious attack on fifth day.

TABLE 5.

EFFECT OF DIFFERENT DIETS ON THE MILK PRODUCTION OF FIVE MOTHERS.

Name	Diet	Milk c.cm.	Sugar %	Fat %	Protein %
Margaret ..	*Institution	1,148	7·83	4·4	1·35
	High protein	1,268	7·53	3·7	1·41
	Home	1,298	7·85	3·9	1·28
	High Protein + Vit. B ..	1,432	7·58	4·1	1·42
	High sugar	1,403	7·67	3·9	1·28
	High fat	1,433	7·47	5·1	1·23
	†Low protein	1,230	7·42	4·6	1·34
Daphne	Institution	1,144	7·66	3·2	1
	High protein	1,298	7·35	3·12	1·2
	Home	1,298	7·37	3·4	1·07
	High protein + Vit. B ..	1,324	7·32	3·4	1·09
	‡High sugar	1,196	7·36	3·35	1·04
	High fat	1,305	7·24	4·0	1·01
	Low protein	1,343	7·34	3·94	·98
Flossie	Institution	694	7·27	3·9	1
	High protein	690	7·34	3·0	1·05
	Home	653	7·58	3·3	·86
	High protein + Vit. B ..	758	7·35	3·7	1·05
	High sugar	630	7·37	3·8	·98
	High fat	683	7·14	4·03	1·03
	Low protein	638	7·38	3·96	·89
Mona	Institution	908	7·87	3·6	1·03
	High protein	930	7·47	3·5	1·17
	Home	855	7·48	3·8	·98
	High protein + Vit. B ..	930	7·42	3·5	1·07
	High sugar	1,058	7·35	3·8	·96
	High fat	885	7·27	4·39	·98
	Low protein	878	7·24	4·32	1·02
Nancy	Institution	743	7·71	3·8	1·44
	High protein	998	7·38	3·5	1·46
	Home	908	7·38	3·3	1·23
	High protein + Vit. B ..	1,013	7·34	3·6	1·3
	High sugar	1,035	7·32	3·4	1·28
	High fat	1,073	7·3	3·99	1·22
	Low protein	998	7·42	3·97	1·19

*Institution diet refers to the ordinary routine diet used in St. Mary's Home.

†This girl was profoundly upset by the death of her father on the day this set of samples was taken.

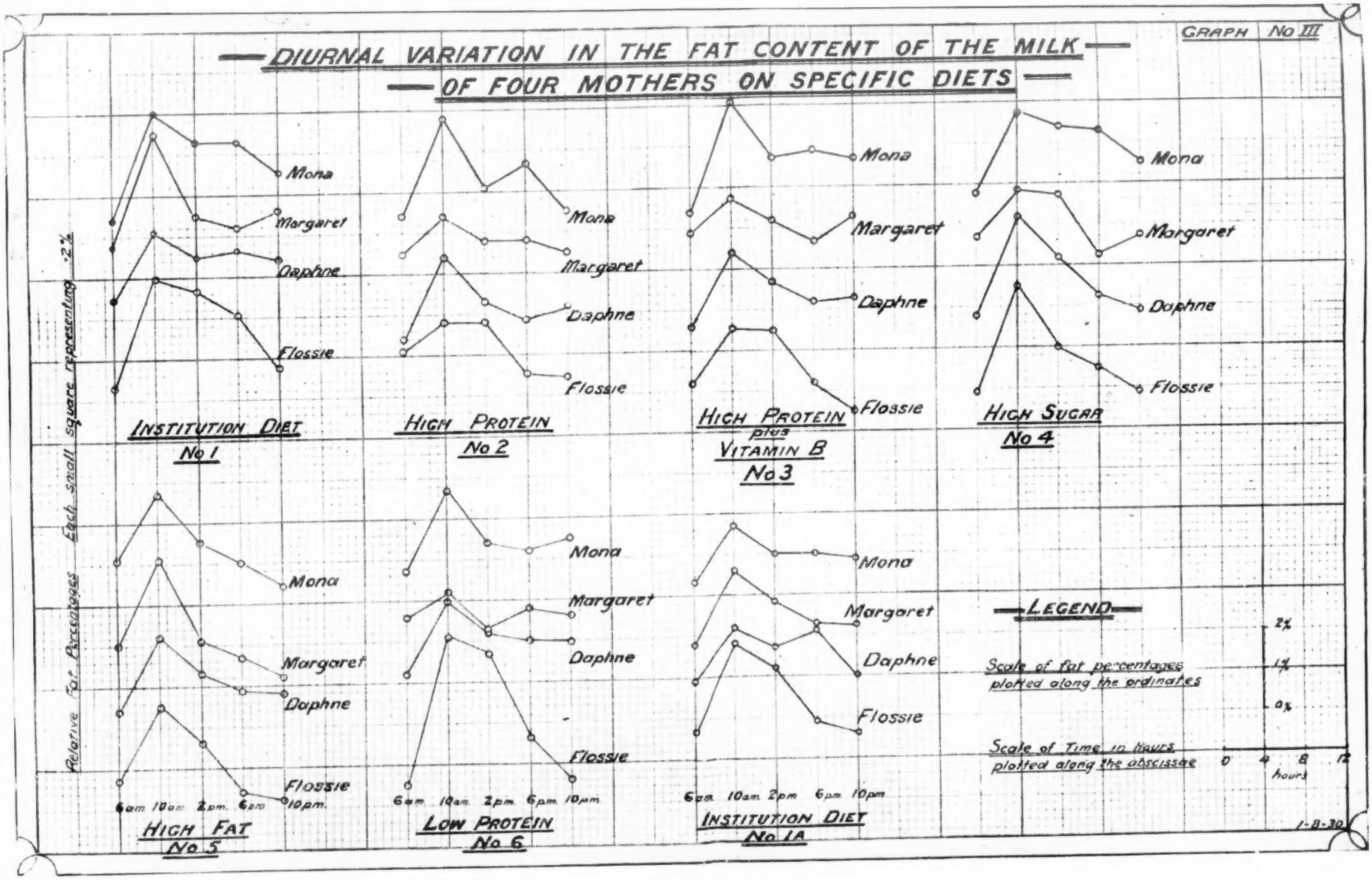
‡This girl had a bilious attack (which prevented her eating) on the day this set of samples was taken.

TABLE 6.

DIURNAL VARIATION IN THE FAT CONTENT OF THE MILK OF FIVE MOTHERS ON DIFFERENT DIETS.

Name	Diet	6 a.m. %	10 a.m. %	2 p.m. %	6 p.m. %	11 p.m. %	Average %
Margaret	Institution	3·75	6·5	4·5	4·2	4·6	4·4
	High protein	3·45	4·5	3·8	3·8	3·5	3·7
	,, ,, +Vit. B	3·9	4·75	4·2	3·65	4·3	4·1
	High sugar	3·7	4·85	4·75	3·25	3·75	3·9
	High fat	5·0	7·1	5·1	4·7	4·2	5·09
	Low protein	4·6	5·2	4·3	4·8	4·6	4·6
	Average	4·06	5·48	4·44	4·06	4·16	4·29
Daphne	Institution	2·5	4·1	3·5	3·65	3·4	3·2
	High protein	2·4	4·4	3·3	2·9	3·1	3·12
	,, ,, +Vit. B	2·6	4·4	3·7	3·2	3·3	3·4
	High sugar	2·8	5·2	4·2	3·25	1·9	3·35
	High fat	3·4	5·2	4·3	3·9	3·8	4·04
	Low protein	3·2	5·0	4·2	4·0	3·95	3·95
	Average	2·82	4·72	3·86	3·48	3·24	3·51
Flossie	Institution	2·3	4·95	4·65	4·05	2·75	3·9
	High protein	3·1	3·8	3·8	2·55	2·45	3·0
	,, ,, +Vit. B	3·2	4·55	4·5	3·2	3·5	3·7
	High sugar	2·9	5·5	4·0	3·5	2·9	3·66
	High fat	3·7	5·5	4·6	3·4	3·2	4·03
	Low protein	2·5	6·1	5·7	3·6	2·6	3·96
	Average	2·95	5·06	4·54	3·38	2·9	3·71
Mona	Institution	2·4	5·0	4·3	4·3	3·5	3·6
	High protein	2·4	4·8	3·1	3·7	2·5	3·3
	,, ,, +Vit. B	2·4	5·1	3·7	3·9	3·7	3·5
	High sugar	2·8	4·75	4·4	4·3	3·5	3·8
	High fat	4·1	5·7	4·5	4·0	3·4	4·39
	Low protein	3·75	5·7	4·4	4·1	4·5	4·32
	Average	2·97	5·18	4·06	4·05	3·51	3·81
		6 a.m.	9 a.m.	12	3 p.m.	6 p.m.	11 p.m.	Av. %
*Nancy	Institution	3·6	5·1	4·2	3·35	3·6	3·15	3·8
	High protein	3·45	4·7	3·4	3·5	3·1	2·9	3·5
	,, ,, +Vit. B ..	3·3	4·65	3·5	3·3	3·1	3·85	3·6
	High sugar	3·3	5·0	3·7	3·1	2·7	2·9	3·4
	High fat	4·3	5·1	3·7	2·65	3·75	3·75	3·99
	Low protein	3·5	5·0	4·3	3·6	3·75	3·85	3·97
	Average ..	3·57	4·93	3·8	3·25	3·33	3·4	3·71

*It will be noted that with the fifth case, Nancy, the milk was expressed at three-hourly intervals throughout the day and the last specimen for the day was collected at 11 p.m.


GRAPH No III
DIURNAL VARIATION IN THE FAT CONTENT OF THE MILK
OF FOUR MOTHERS ON SPECIFIC DIETS
Relative Fat Percentages Each small square representing .2%
Mona
Margaret
Daphne
Flossie
INSTITUTION DIET No 1
HIGH PROTEIN No 2
HIGH PROTEIN plus VITAMIN B No 3
HIGH SUGAR No 4
HIGH FAT No 5
LOW PROTEIN No 6
INSTITUTION DIET No 1A
6am 10am 2pm 6pm 10pm
LEGEND
Scale of fat percentages plotted along the ordinates
2%
1%
0%
Scale of Time in hours plotted along the abscissae
0 4 8 12
hours
1-8-30

GRAPH III.

Discussion of results.

In the following summary the results obtained at the end of one week's dieting have been compared with those obtained at the end of the previous week.

1. High protein diet. (A) EFFECT ON MILK YIELD.—Four of the five mothers showed an increase in the twenty-four hourly yield compared with that obtained on the Institution diet. The average increase in amount was 108 c.cm.

(B) EFFECT ON COMPOSITION.—There was a slight increase in the protein percentage of the milk in every case. The average increase was ·09 per cent.

In each case the fat percentage of the milk was reduced.

When the high protein diet was followed by the Institution diet a marked decrease (averaging ·17 per cent.) in the protein percentage of the milk was noticed. In all cases but one, the protein percentage fell below that present at the initiation of the experiments. In two of the five cases the increased milk yield noted in the previous week was maintained, but in three cases the yield was diminished.

2. High protein diet plus Vitamin B.—This diet appeared to produce an increase in the twenty-four hourly yield in every case. The average increase compared with the previous week's yield was 88·5 c.cm. The protein percentage of the milk was again increased: the average increase compared with the previous week was ·1 per cent.

3. High carbohydrate Diet.—Three mothers showed a slight decrease in the yield compared with that of the previous week. One showed a marked increase.

The composition of the milk was much the same as it was when the mothers were fed on the Institution diet.

4. High fat diet.—In general the milk yield was increased very slightly as compared with the amounts obtained on the previous diet. The composition of the milk was strikingly affected. In every case, the fat percentage of the milk was increased. The average increase on the previous week's fat percentage was ·6 per cent., and the average increase in the total amount of fat produced was 20 per cent.

5. Low protein diet.—In general there was a slight diminution in the yield compared with that obtained in the previous week. One case, Case 1*, which should, perhaps, be eliminated, showed a marked diminution in amount, and one (Case 2) actually showed an increase.

The composition of the milk was very little affected. In three cases, the protein percentage compared with that of the previous week was slightly lowered; in two cases it was actually raised.

Discussion.—The increase obtained in the fat percentage of the milk when the mothers were on a high fat diet was very definite. This finding, though

*This subject was profoundly upset by the death of her father on the day the samples were taken.

contrary to the general opinion of dairy scientists in respect to cows, agrees with the practical observations of the Plunket nurses (Truby King system) throughout New Zealand. They state that idle mothers who over-indulge in rich fatty foods invariably have milk with a high fat content. Careful analyses of the milk of such mothers fully supports this statement. Moreover, it has been found that this high fat percentage can be reduced by systematic dieting.

The yield of milk was strikingly increased when mothers were fed on a high protein diet. This conclusion is in accordance with the results of observations made on cows. It also agrees with Hoobler's contention in respect to human milk production. The yield of milk remained either stationary or was lessened when the high protein diet was followed by the Institution diet.

The feeding of the high protein diet plus Vitamin B again produced a marked increase in the milk yield.

It is interesting to note that women who were fed on exactly similar diets showed marked differences in respect to the average fat percentage of their milk. The high fat percentage is evidently a personal characteristic as in the case of cows.

Babies receiving milks of such vastly different fat content throve equally well. When the fat percentage of the milk was raised as the result of the high fat diet given to the mother, the babies were not digestively upset. This, in a measure, may be due to the fact that the mothers were healthy and continuously engaged in manual work.

The 28 graphs illustrating the diurnal variation in the fat content of the milk of the four mothers fed on the six specific diets above mentioned, show that the generalization arrived at in Part I of this paper still holds even when there is a great variation in the diet of the mother. The fat content in every case was highest at 10 a.m. and the diurnal variation in general agreement with the previous findings. Once again it was observed that the milks of high average fat content had the greatest diurnal variation.

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Summary of Part II.

The effects of different diets on the milk secretion of women have been studied.

1. The feeding of a high fat diet to nursing mothers was found to increase the fat percentage of their milk.
2. The feeding of a high protein diet and a high protein plus Vitamin-B diet was found to increase the milk yield.

3. The composition of the milk was not appreciably affected by great changes in the constituents of the diet other than fat.

4. The results of 28 determinations of the diurnal variation in the fat content of human milk are tabulated and recorded graphically. The results support the generalization arrived at in Part I of this paper.

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OTITIS MEDIA WITH PURULENT MENINGITIS IN AN INFANT NINE DAYS OLD

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Purulent meningitis arising from otitis media in very young infants is a rare condition. The case we record is the only one which has occurred in the Obstetric Hospital, University College Hospital, during the last four years. Cruickshank[1] in his investigation of 800 neonatal deaths, (i.e., in infants up to 28 days old), found meningitis in 4 per cent. of the cases. He, however, does not describe any cases associated with otitis media.

The condition of otitis media in newly born and young infants is well recognized, particularly by French observers.

Duverney[2] in 1683 was the first to point out the presence of fluid in the middle ear in these infants. Schmaltz[3], Lesser[4] and Lenhardt[5] drew attention to the presence of vernix caseosa and liquor amnii in the middle ear. Kopper[6] in 1857 was the first to note the presence of pus. In a number of infants aged less than 25 days he noted an empty space 6 times and the presence of fluid in 18 cases, in 4 of which the fluid had the character of pus. Schwartze[7], Roosa[8], de Troeltsch[9], Parrot[10] and Wendt[11] were also among the early observers of this condition and since their time numerous cases have been recorded.

There is disagreement whether the otitis media is a primary or secondary infection. Hartmann[12], Byfield[13], Preysing[14], McDougal and Knaker[15], Floyd[16], Alden and Lyman[17], Pluder[18] and other authors note the co-existence of gastro-intestinal or respiratory disease with otitis media. These observers believe that the otitis precedes the enteritis or respiratory disease in certain cases. They believe that an aggravation of the otitis causes an aggravation of the enteritis. They show the necessity for paracentesis and cite cases where clinical signs have disappeared when paracentesis is performed. On the other hand, Lenhartz[19], Veillard[20] and others who also note the same association of otitis media with gastro-enteritis or respiratory disease, believe that the otitis is an agonal infection.

Mahu and Chomé[21] report a case of still-born fœtus, where they believe the middle ear was infected during labour. The mother was a primipara; presentation was breech; duration of labour 48 hours; membranes ruptured at commencement of labour. On post-mortem examination the middle ear was found infected. Cultures were taken from the middle ear. According to Mahu and Chomé the anatomical state of the ear in the fœtus and the infant at birth is such that there is an anatomical predisposition to infection. The Eustachian tube has not yet reached its full development and is short and wide. The tympanic cavity is filled by a gelatinous material which opposes no

obstacle to the penetration of liquids and offers on the other hand an excellent culture medium to micro-organisms which can penetrate. The infections occur at the moment of aspiration and deglutition. When in the process of birth the fœtus inspires, the contents of the maternal vagina move towards the fœtal lung ; but if the movement of deglutition intervenes the contents of the maternal vagina are forced towards the middle ear, penetrate the gelatinous material, dislocate it and gradually transform the tympanic cavity into a real cavity.

The rarity of perforation of the drum is noted by all observers. Arbeltier[22] showed that in a series of 125 infants aged 1 to 20 months in l'Hôpital Bretonneau, 11 had a discharge from one or other ear, i.e., 8·8 per cent. In the same hospital when a systematic examination of the ears was made in a series of 102 infants of the same age period, 72 infants were found to have otitis, which was often bilateral, i.e., 72 per cent. In a series of 150 infants examined in the out-patient department of the same hospital 33 per cent. had otitis. Alden and Lyman[23], in a series of 70 consecutive autopsies on infants who died of vomiting and infantile diarrhœa, found suppuration in the middle ear in all cases. Thirty cases had been diagnosed during life.

The absence of meningitis in cases of otitis media in newly born infants is also noted. Veillard[20] in a series of 80 cases of otitis media did not meet with one case. Goeppert[24] has stated that the danger of meningitis and septicæmia as a result of otitis is less in infants than in adults. Netter[25] found bilateral otitis media in 20 cases ; post mortem, among these cases there were two instances of suppurative meningitis. Thrombosis of the inferior petrosal sinus is also rare and the only record I have been able to find is one by Renaud[26] in a six weeks old child.

Case report.

The importance and rarity of otitis media in the causation of death in the new-born seem sufficient justification for recording the following case.

The mother, a 4-para aged 35 years, had a normal pregnancy and had been under observation at the ante-natal clinic during the last two months of her pregnancy. Her Wassermann reaction was negative. She was admitted to the Obstetric Hospital, University College Hospital, on September 11th, 1930. The history of the labour was as follows : labour pains commenced at 5 a.m., September 11th, membranes ruptured at the same time. The child, full time, was delivered spontaneously at 1·25 a.m., September 12th. The presentation was left occipito-anterior. Weight at birth was 3,650 grm.

During the first 5 days the baby appeared perfectly normal; temperature, pulse and respirations were normal. On 3rd and 4th days the infant gained in weight. On the 6th day the cord separated, the temperature rose to 100·2° and respirations were rapid, but the infant took his feeds. On the 7th day the temperature was 101°, respirations 40, and feeds were not being well taken. The mother's milk was expressed and given in a bottle. On the 8th day the temperature was 101°, and respirations irregular, Cheyne Stokes in type. The infant was slightly jaundiced and refused feeds ; he was not sick and his stools were normal. The thorax was examined but no abnormal physical signs were discovered. There was no head retraction ; the fontanelle was not tense. There was no discharge from the ears. On the 9th day the temperature was 101° and in the morning the general condition seemed better and he took breast milk occasionally, but in the afternoon he had several attacks of dyspnœa, refused to take feeds and died at 11 p.m.

POST-MORTEM EXAMINATION.—Full time male infant, slightly jaundiced; no evidence of emaciation; umbilical cord separated and no evidence of sepsis around the scar. Weight of infant was 3,050 grm., length 51 cm. The thymus was very pale but normal in size. The lungs were fully aerated and congested, but there was no consolidation and no naked eye evidence of pneumonia. Microscopically the lungs were congested and in one area there was a slight small celled infiltration, but no exudate. The heart was normal in size, but looked paler than normal and fatty. There was no valvular lesion. Nothing abnormal was noted in the abdominal cavity beyond the toxic appearance of all the organs. The umbilical scar appeared healthy and on sectioning there was no evidence of infection.

On examining the brain there were found marked congestion of the meninges and a considerable amount of greenish pus on all surfaces of the cerebral hemispheres, but most marked round the base of the brain. The right ear showed no abnormality; the left ear, middle ear and surrounding bone were soft and filled with greenish pus. Cultures were taken from the brain and middle ear and a profuse mixed growth was obtained. The causal organism could not be isolated.

Summary.

A case of primary otitis media with purulent meningitis in a newly born infant is reported.

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